Access DB# 21516

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: HARDY Examiner # : 1236 Date: 4/16/03
Art Unit: 1751 Phone Number 305-5589 Serial Number: 09/914,942
Mail Box and Bldg/Room Location: 9B36 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

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Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): _____

_____

Earliest Priority Filing Date: _____

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Whatever you can find. Thanks.

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STAFF USE ONLY	Type of Search		Vendors and cost where applicable	
Searcher: EA	NA Sequence (#)		STN	$258.25
Searcher Phone #:	AA Sequence (#)		Dialog	
Searcher Location:	Structure (#)	1 (c) (Markush)	Questel/Orbit	
Date Searcher Picked Up:	Bibliographic		Dr.Link	
Date Completed: 4.17.03	Litigation		Lexis/Nexis	
Searcher Prep & Review Time: 20	Fulltext		Sequence Systems	
Clerical Prep Time:	Patent Family		WWW/Internet	
Online Time: 115	Other		Other (specify)	

PTO-1590 (8-01)

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=> d his


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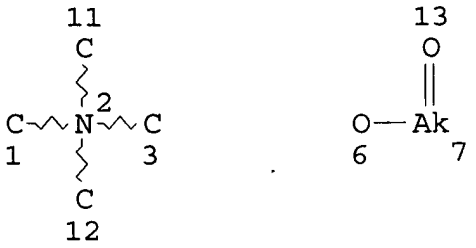

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GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 8

STEREO ATTRIBUTES: NONE
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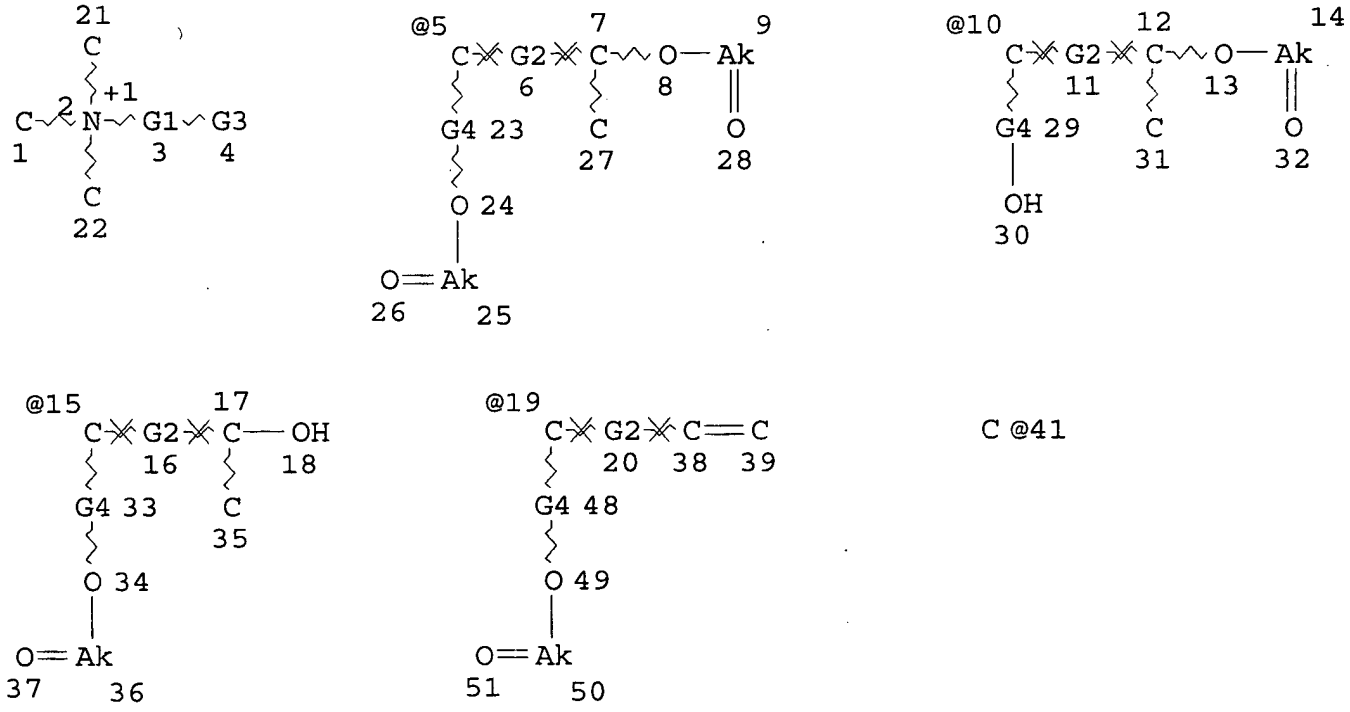

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GRAPH ATTRIBUTES:
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NUMBER OF NODES IS  44

STEREO ATTRIBUTES: NONE
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100.0% PROCESSED  7651 ITERATIONS                          5 ANSWERS
SEARCH TIME: 00.00.02


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FILE 'ZCAPLUS' ENTERED AT 13:11:52 ON 17 APR 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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=> d l17 1 ibib abs hitstr hitrn

L17  ANSWER 1 OF 1  ZCAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         2000:645980  ZCAPLUS
DOCUMENT NUMBER:          133:239741
TITLE:                    Esterquats, their intermediates, a process to
                          make the esterquats, and their use as fabric
                          softeners
```

INVENTOR(S): Ahrens, Hartmut; Bergfeld, Manfred Josef
PATENT ASSIGNEE(S): Akzo Nobel N.V., Neth.
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000053570	A1	20000914	WO 2000-EP1738	20000228
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1159257	A1	20011205	EP 2000-909277	20000228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002539111	T2	20021119	JP 2000-604011	20000228

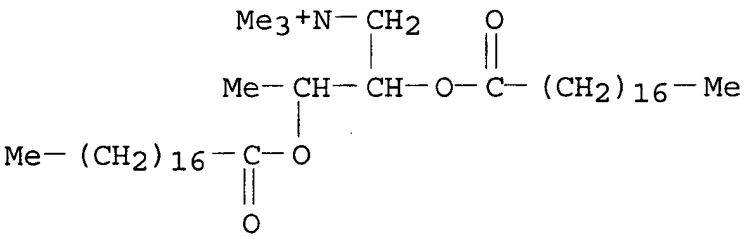
PRIORITY APPLN. INFO.: EP 1999-200638 A 19990305
WO 2000-EP1738 W 20000228

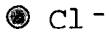
OTHER SOURCE(S): MARPAT 133:239741

AB The title esterquats are of the formula: R4[R5R6N+Z]n X-, wherein Z is covalently bonded to the nitrogen atom and selected from various specified ester-contg. groups, R4 is C1-6 alkyl or independent Z, R5 is H, C1-6 alkyl, independent Z, or the residue of the quaternizing agent, such as C1-30 alkyl or alkenyl, preferably, C1-7 alkyl or alkenyl, R6 is C1-6 alkyl or independent Z, and X- is an ion selected from Cl-, Br-, I-, F-, CH3SO4-, C2H5SO4-, H2PO4-, HPO42-, PO43-, H2PO3-, HPO32-, H2PO2-, HPO22-, nitrate-, formate-, acetate-, propionate-, tartrate- and benzoate-, wherein the total charge of the anions equals the total charge of the cations.

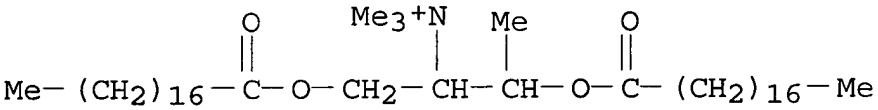
IT **293729-71-2P 293729-72-3P**
(esterquats, their intermediates, a process to make the esterquats, and their use as fabric softeners)

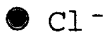
RN 293729-71-2 ZCAPLUS
CN 1-Butanaminium, N,N,N-trimethyl-2,3-bis[(1-oxooctadecyl)oxy]-, chloride (9CI) (CA INDEX NAME)





RN 293729-72-3 ZCAPLUS
CN 2-Butanaminium, N,N,N-trimethyl-1,3-bis[(1-oxooctadecyl)oxy]-, chloride (9CI) (CA INDEX NAME)





IT **293729-71-2P 293729-72-3P**
(esterquats, their intermediates, a process to make the esterquats, and their use as fabric softeners)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l19 1-25 cbib abs hitstr hitrn

L19 ANSWER 1 OF 25 ZCAPLUS COPYRIGHT 2003 ACS
2002:648412 Document No. 137:174974 Liposome vectors containing sterol glucosides for hepatocyte targeting gene therapy, and method for manufacturing thereof. Ui, Seiki; Yonetani, Yoshie; Takayama, Kozo (Ryukakusan Co., Ltd., Japan). Jpn. Kokai Tokkyo Koho JP 2002241313 A2 20020828, 8 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 2001-38768 20010215.
AB The invention provides a liposome vector contg. sterol glucoside for use for hepatocyte targeting gene therapy. Sterol glucoside (SG) consisting of .beta.-sitosteryl-.beta.-D-glucoside 49.9, campesteryl-.beta.-D-glucoside 29.1, stigmasteryl-.beta.-D-glucoside 13.4, brassicasteryl-.beta.-D-glucoside 7.2 % was prepd. Luciferase

plasmid DNA-encapsulated liposomes were prepd. from dipalmitoylphosphatidylcholine, cholesterol, and SG (6:3:1), and its gene expression in human hepatoma HepG2 cells was examd.

IT **188565-00-6**, Tfx-20
(liposome vectors contg. sterol glucosides for hepatocyte targeting gene therapy)

RN 188565-00-6 ZCAPLUS

CN 1,4-Butanediaminium, N,N'-bis(2-hydroxyethyl)-N,N,N',N'-tetramethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, diiodide, mixt. with 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl di-(9Z)-9-octadecenoate (9CI) (CA INDEX NAME)

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CRN 219304-09-3
CMF C48 H94 N2 O6 . 2 I

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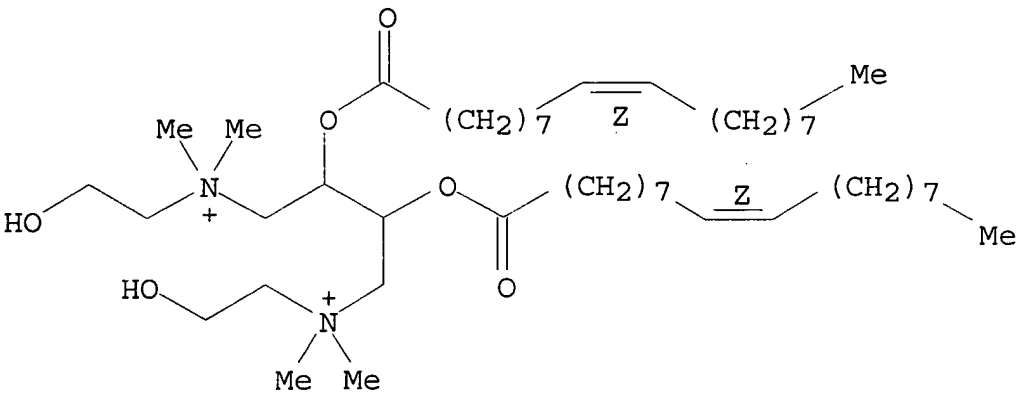


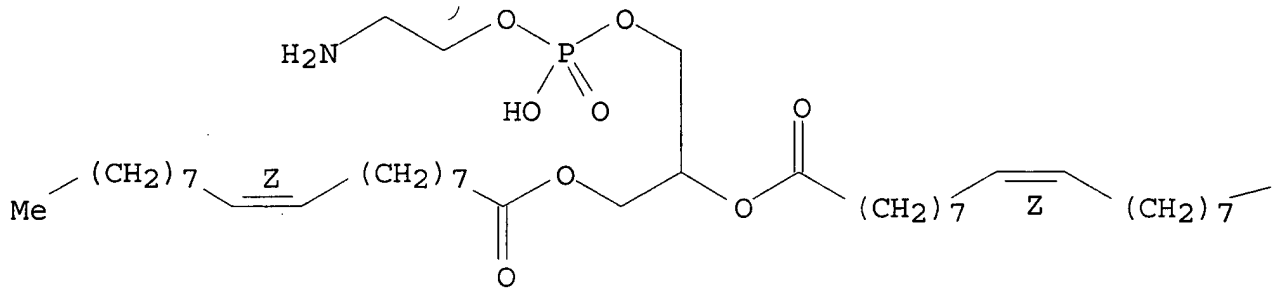
●2 I^-

CM 2

CRN 2462-63-7
CMF C41 H78 N O8 P

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

IT **188565-00-6**, Tfx-20
(liposome vectors contg. sterol glucosides for hepatocyte targeting gene therapy)

L19 ANSWER 2 OF 25 ZCAPLUS COPYRIGHT 2003 ACS
2002:199221 Document No. 137:57284 Optimization of nonviral gene transfer of vascular smooth muscle cells in vitro and in vivo. Armeanu, Sorin; Pelisek, Jaroslav; Krausz, Eberhard; Fuchs, Alexandra; Groth, Detlef; Curth, Rene; Keil, Oliver; Quilici, Jacques; Rolland, Pierre H.; Reszka, Regina; Nikol, Sigrid (Medical Clinic I, Klinikum Grosshadern, Ludwig Maximilian University, Munich, D-81377, Germany). Molecular Therapy, 1(4), 366-375 (English) 2000. CODEN: MTOHCK. ISSN: 1525-0016. Publisher: Academic Press.

AB Gene therapy strategies for the prevention of restenosis postangioplasty are promising. Nonviral gene transfer to the arterial wall in vivo has so far been limited by poor efficiency. This study aimed to optimize transfection of primary vascular smooth muscle cells using cationic nonviral formulations based on cholesterol derivs. (DC-, DAC-, DCQ-, and Sp-Chol), double-chained amphiphiles (LipofectAMINE, DOTMA, DOSGA, DOSPER, and DOCSPER), or heterogeneous reagents (Superfect, Effectene, and Tfx-50). Estn. of transfection efficiencies was performed using galactosidase assays at different ratios of transfection reagent to plasmid DNA with reporter gene. Toxicity was monitored by analyzing cell metab. Transfer efficiency and safety were detd. in a porcine restenosis model for local gene therapy using morphometry, histol.,

galactosidase assays, and reverse-transcriptase polymerase chain reaction. The highest in vitro transfection efficiency was achieved using the recently developed DOCSPER liposomes, with transfer rates of at least 20% in vascular smooth muscle cells. Transfer efficiency was further enhanced up to 20% by complexing with poly-L-lysine. Transfection efficiency in vivo in a porcine restenosis model was up to 15% of adventitial cells using DOCSPER vs. 0.1% using LipofectAMINE. Toxicity in vivo and in vitro was lowest using DOCSPER. Increased biol. effects were demonstrated following optimization of transfer conditions. (c) 2000 Academic Press.

IT **188565-00-6**, Tfx-50
(optimization of nonviral gene transfer of vascular smooth muscle cells in vitro and in vivo)

RN 188565-00-6 ZCAPLUS

CN 1,4-Butanediaminium, N,N'-bis(2-hydroxyethyl)-N,N,N',N'-tetramethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, diiodide, mixt. with 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl di-(9Z)-9-octadecenoate (9CI) (CA INDEX NAME)

CM 1

CRN 219304-09-3
CMF C48 H94 N2 O6 . 2 I

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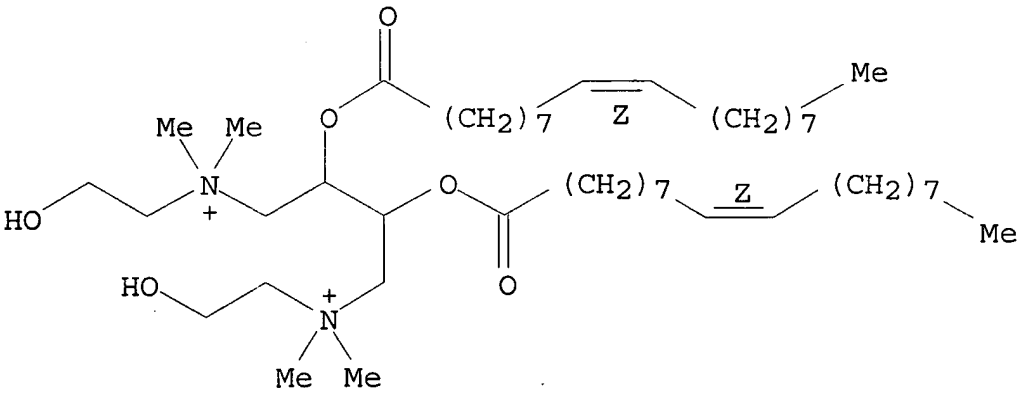


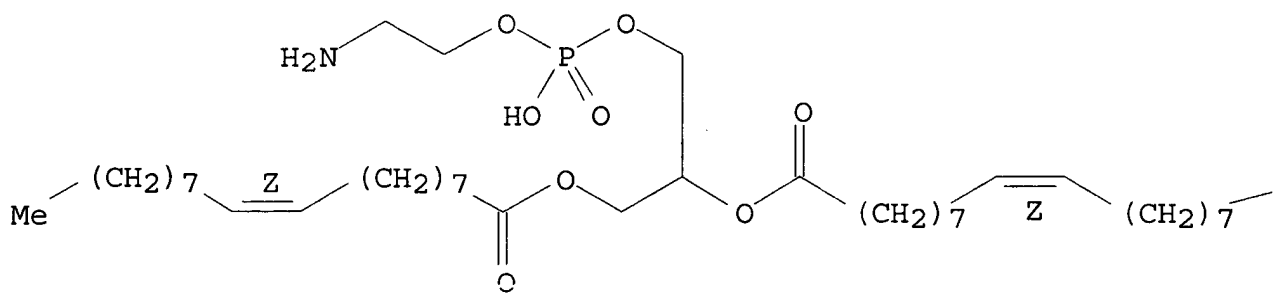
● 2 I⁻

CM 2

CRN 2462-63-7
CMF C41 H78 N O8 P

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

IT **188565-00-6**, Tfx-50
(optimization of nonviral gene transfer of vascular smooth muscle cells in vitro and in vivo)

L19 ANSWER 3 OF 25 ZCAPLUS COPYRIGHT 2003 ACS
2001:906205 Document No. 136:42809 Method for nucleic acid transfection of cells using cationic lipid/DNA complex. Bennett, Michael J.; Rothman, Stephan S.; Nantz, Michael H. (USA). U.S. Pat. Appl. Publ. US 2001051610 A1 20011213, 26 pp., Cont.-in-part of U. S. Ser. No. 487,089. (English). CODEN: USXXCO. APPLICATION: US 2001-766320 20010118. PRIORITY: US 2000-487089 20000119.

AB The present invention describes methods for introducing nucleic acids into a target cell using a transition metal enhancer. A mixt. contg. nucleic acid and a transition metal enhancer is exposed to cells. The nucleic acid is taken up into the interior of the cell with the aid of the transition metal enhancer. The transition metal enhancer tested includes zinc, nickel, cobalt and copper in animal cell line, or rat salivary gland or mouse lung. It is shown zinc can enhance both in vitro and in vivo transfection of liposome/DNA mixt. depending on the cationic lipid to nucleic acid charge ratio. Since nucleic acids can encode a gene, the method can be used to replace a missing or defective gene in the cell. The method can also be used to deliver exogenous nucleic acids operatively coding for proteins that are secreted or released from target cells, thus resulting in a desired biol. effect outside the cell. Alternatively, the methods of the present invention can be used to

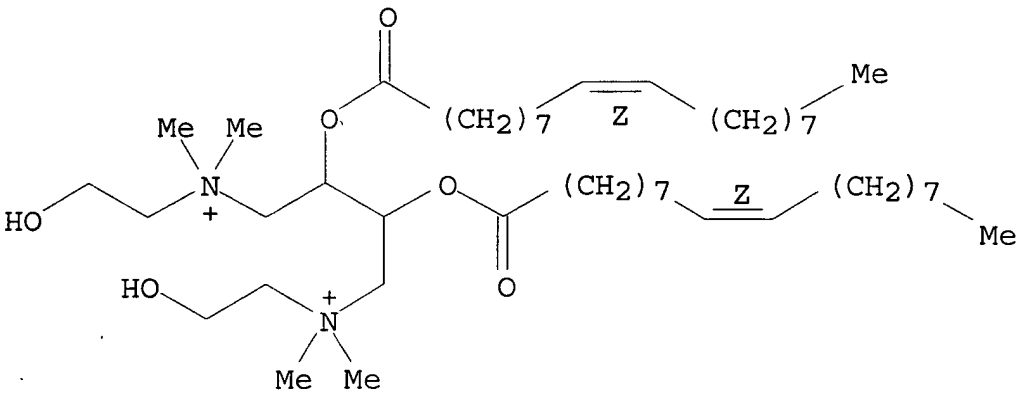
deliver exogenous nucleic acids into a target cell that are capable of regulating the expression of a predetd. endogenous gene. This can be accomplished by encoding the predetd. endogenous gene on the nucleic acid or by encoding the nucleic acid with a sequence that is the Watson-Crick complement of the mRNA corresponding to the endogenous gene.

IT **219304-09-3**
(method for nucleic acid transfection of cells using cationic lipid/DNA complex)

RN 219304-09-3 ZCAPLUS

CN 1,4-Butanediaminium, N,N'-bis(2-hydroxyethyl)-N,N,N',N'-tetramethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, diiodide (9CI) (CA INDEX NAME)

Double bond geometry as shown.



● 2 I^-

IT **219304-09-3**
(method for nucleic acid transfection of cells using cationic lipid/DNA complex)

L19 ANSWER 4 OF 25 ZCAPLUS COPYRIGHT 2003 ACS

2001:743555 Document No. 137:67998 Development of Efficient Transient Transfection Systems for Introducing Antisense Oligonucleotides into Human Epithelial Skin Cells. Fimmel, Sabine; Saborowski, Antje; Orfanos, Constantin E.; Zouboulis, Christos C. (Department of Dermatology, University Medical Center Benjamin Franklin, The Free University of Berlin, Berlin, Germany). Hormone Research, Volume Date 2000, 54(5-6), 306-311 (English) 2001. CODEN: HRMRA3. ISSN: 0301-0163. Publisher: S. Karger AG.

AB Systemic treatment with antisense oligonucleotides is confounded by the dual problems of potential cytotoxicity of antisense oligonucleotides and carrier mols. such as cationic lipids. Treatment of pathol. conditions affecting the skin may avoid these

problems to a large degree due to local application. The success of antisense strategies has been limited by the poor uptake of the transfection reagent and inadequate intracellular compartmentalization. Human skin epithelial cells, therefore, are attractive exptl. tools for testing both in vitro and in vivo antisense therapies. In the present study, we detd. com. available liposomes which reproducibly induced a nontoxic increase of oligonucleotide uptake in cultured SZ95 sebocytes and keratinocytes. The final protocol for SZ95 sebocytes was a 4-h incubation with DOTAP in a 2:1 (wt./wt.) lipid/oligonucleotide ratio in serum-free medium. The fluorescein-labeled (ATCG)5 random oligonucleotide mols. were detected within the nucleus. The optimum transfection system for primary keratinocytes was poly-L-ornithine (12 .mu.g/mL) in a medium without bovine pituitary ext. over 4 h. The uptake of the oligonucleotide increased in the presence of the polycation and oligonucleotide mols. were localized in the cytoplasm of keratinocytes. Oligonucleotide transfection with the help of cationic lipids did not affect the expression of androgen receptor and of the house-keeping gene .beta.-actin. Thus, cationic lipids are useful for delivery of antisense oligonucleotides into skin cells in vitro and may be used for topical cationic lipid application on animal and human skin.

IT **188565-00-6**, Tfx-10
(cationic lipids effect on transfection of antisense oligonucleotides into human epithelial skin cells)

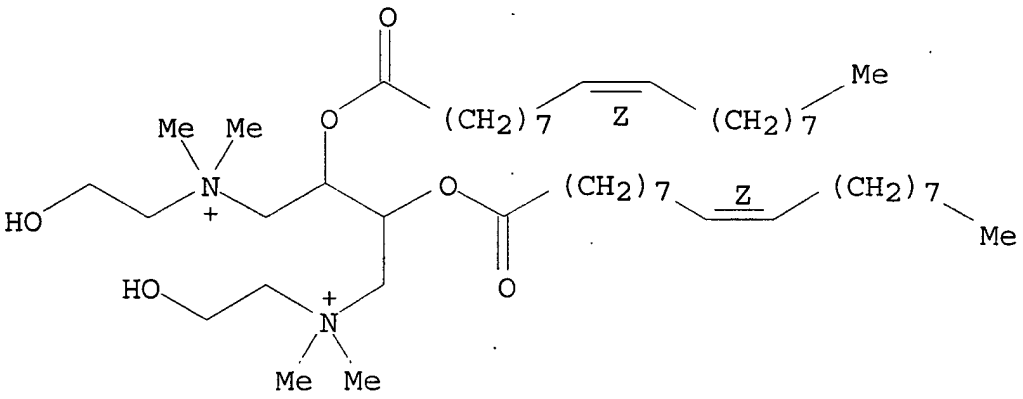
RN 188565-00-6 ZCAPLUS

CN 1,4-Butanediaminium, N,N'-bis(2-hydroxyethyl)-N,N,N',N'-tetramethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, diiodide, mixt. with 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl di-(9Z)-9-octadecenoate (9CI) (CA INDEX NAME)

CM 1

CRN 219304-09-3
CMF C48 H94 N2 O6 . 2 I

Double bond geometry as shown.



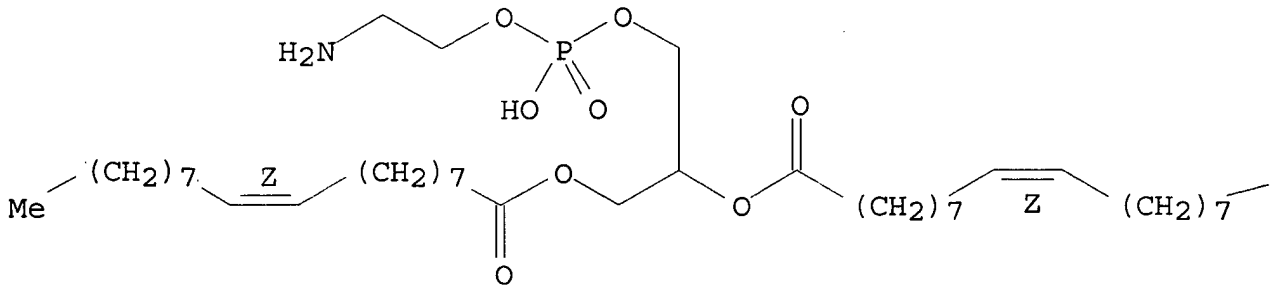
●2 I^-

CM 2

CRN 2462-63-7
CMF C41 H78 N O8 P

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

IT **188565-00-6**, Tfx-10
(cationic lipids effect on transfection of antisense oligonucleotides into human epithelial skin cells)

L19 ANSWER 5 OF 25 ZCAPLUS COPYRIGHT 2003 ACS
2001:613441 Document No. 135:376637 Liver-targeted gene transfer into a human hepatoblastoma cell line and in vivo by sterylglucoside-containing cationic liposomes. Hwang, S. H.; Hayashi, K.; Takayama, K.; Maitani, Y. (Department of Pharmaceutics, Hoshi University, Tokyo, Japan). Gene Therapy, 8(16), 1276-1280 (English) 2001. CODEN: GETHEC. ISSN: 0969-7128. Publisher: Nature Publishing Group.

AB We investigated the transfection efficiency of .beta.-sitosterol .beta.-D-glucoside (Sit-G)-contg. liposome/DNA complex (Sit-G-liposome/DNA complex) for liver targeting. The Sit-G-liposome/DNA complex was composed of Tfx-20 reagent (Tfx), ie synthetic cationic lipid [N,N,N',N'-tetramethyl-N,N'-bis(2-hydroxyethyl)-2,3-di(oleoyloxy)-1,4-butanediammonium iodide] with L-dioleoylphosphatidylethanolamine (DOPE), 3.beta.[N-(N',N'-dimethylaminoethane)-carbamoyl]cholesterol (DC-Chol) and Sit-G with plasmid DNA. The in vitro studies were performed in HepG2 cells in serum-contg. medium and the in vivo studies were carried out in the mice following i.v. injection. The Sit-G-liposome produced a Sit-G-liposome/DNA complex of relatively small size (100-250 nm). Transfection efficiency of the luciferase marker gene by Sit-G-liposome/DNA complex was increased in the presence of 10% serum in vitro, and was selectively high in the mouse liver reaching expression values up to an av. of 14.9 pg luciferase/mg tissue protein, compared with Tfx/DNA complex, which showed approx. three-fold higher gene expression than Sit-G-liposome/DNA complex in vitro. High in vitro transfection efficiency by Sit-G-liposome/DNA complex seemed to be possible even with large lipid ppts., whereas high in vivo activity seemed to be related to small and dispersed complexes. The interaction of liposome/DNA complexes with serum may be a key point to predict the in vivo efficiency of a liposome vector.

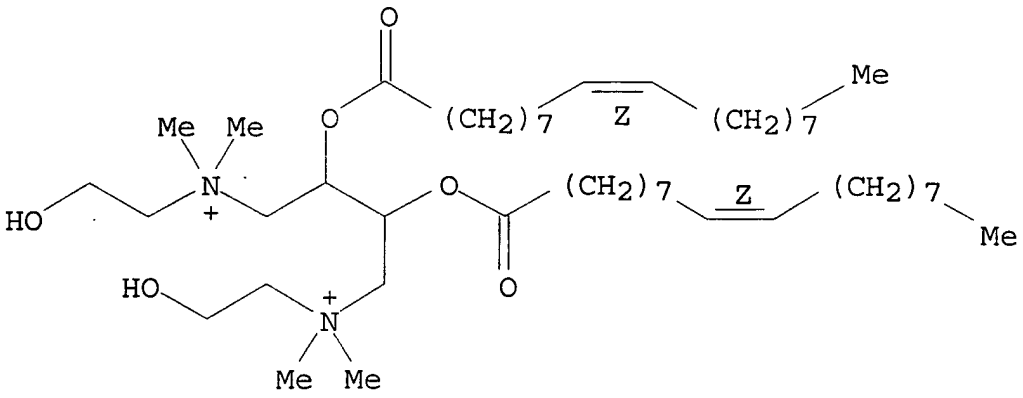
IT **188565-00-6D**, Tfx-20, complexes with DNA
(liver-targeted gene transfer into a human hepatoblastoma cell line and in vivo by sterylglucoside-contg. cationic liposomes)

RN 188565-00-6 ZCAPLUS
CN 1,4-Butanediaminium, N,N'-bis(2-hydroxyethyl)-N,N,N',N'-tetramethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, diiodide, mixt. with 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl di-(9Z)-9-octadecenoate (9CI) (CA INDEX NAME)

CM 1

CRN 219304-09-3
CMF C48 H94 N2 O6 . 2 I

Double bond geometry as shown.



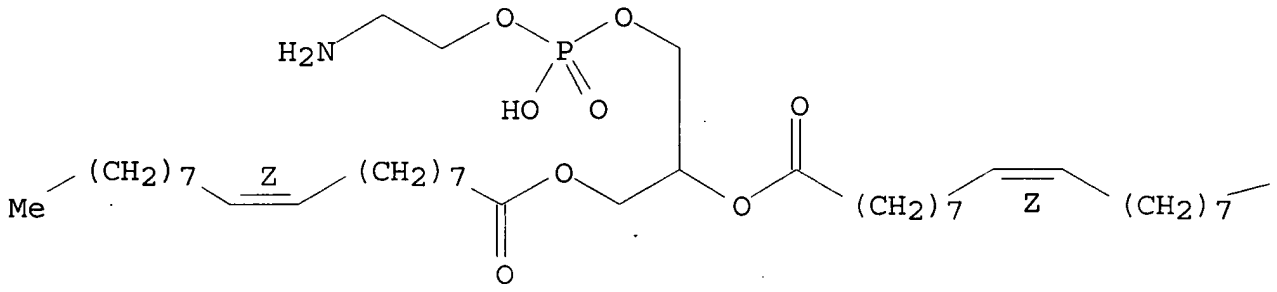
● 2 I^-

CM 2

CRN 2462-63-7
CMF C41 H78 N O8 P

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

IT **188565-00-6D**, Tfx-20, complexes with DNA

(liver-targeted gene transfer into a human hepatoblastoma cell line and in vivo by sterylglucoside-contg. cationic liposomes)

L19 ANSWER 6 OF 25 ZCAPLUS COPYRIGHT 2003 ACS

2001:545533 Document No. 135:127170 Method for nucleic acid transfection of cells. Bennett, Michael J.; Rothman, Stephan S.; Nantz, Michael H. (Genteric, Inc., USA). PCT Int. Appl. WO 2001052903 A1 20010726, 68 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US1803 20010119. PRIORITY: US 2000-487089 20000119; US 2001-766320 20010118.

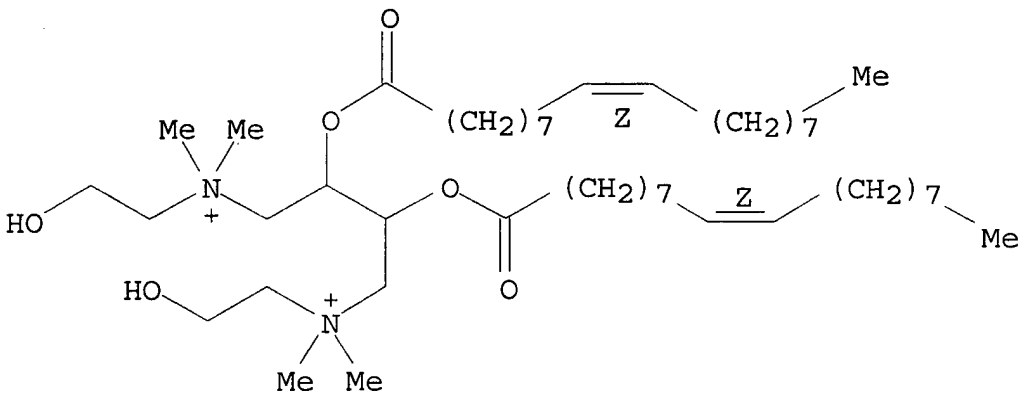
AB The present invention describes methods for introducing nucleic acids into a target cell using a transition metal enhancer. A mixt. contg. nucleic acid and a transition metal enhancer is exposed to cells. The nucleic acid is taken up into the interior of the cell with the aid of the transition metal enhancer such as cobalt. Since nucleic acids can encode a gene, the method can be used to replace a missing or defective gene in the cell. The method can also be used to deliver exogenous nucleic acids operatively coding for proteins that are secreted or released from target cells, thus resulting in a desired biol. effect outside the cell. Alternatively, the methods of the present invention can be used to deliver exogenous nucleic acids into a target cell that are capable of regulating the expression of a predetd. endogenous gene. This can be accomplished by encoding the predetd. endogenous gene on the nucleic acid or by encoding the nucleic acid with a sequence that is the Watson-Crick complement of the mRNA corresponding to the endogenous gene.

IT **219304-09-3**
(transition metal enhancement of nucleic acid transfection of cells)

RN 219304-09-3 ZCAPLUS

CN 1,4-Butanediaminium, N,N'-bis(2-hydroxyethyl)-N,N,N',N'-tetramethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, diiodide (9CI) (CA INDEX NAME)

Double bond geometry as shown.



●2 I^-

IT **219304-09-3**
(transition metal enhancement of nucleic acid transfection of cells)

L19 ANSWER 7 OF 25 ZCAPLUS COPYRIGHT 2003 ACS
2001:338739 Document No. 134:348934 Use of nucleic acid-binding proteins from prokaryotes as vehicles for the delivery of materials to eukaryotic cells. Boehm, Gerald; Esser, Dirk (ACGT Progenomics A.-G., Germany). PCT Int. Appl. WO 2001032900 A1 20010510, 64 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (German). CODEN: PIXXD2. APPLICATION: WO 2000-EP10875 20001103. PRIORITY: DE 1999-19952983 19991103.

AB The invention relates to a method for the transfer of mol. substances, for example proteins or nucleic acids into cells. A prokaryotic nucleic acid-binding protein is used for the transfer, which is preferably obtained from a thermotolerant or thermophilic organism. Where the substance to be transferred is a nucleic acid, the protein forms a reversible complex with the nucleic acid. The prokaryotic protein condenses and compacts the nucleic acids allowing them to be more efficiently taken up by target cells and also protecting them from nucleases. Said nucleic acids can be taken up in the target cells after suitable incubation. The protein may be further modified by adding ligands for cell surface receptors or nuclear localization signals to ensure efficient uptake and transfer to the nucleus. The use of the HU protein of Thermotoga

maritima manufd. in Escherichia coli is described., The protein protected complexed nucleic acids from nucleases in vitro and was not toxic to animal cells.

IT **188565-00-6**, TFX 50
(liposomes of, contg. protein DNA complexes, for transformation of animal cells; use of nucleic acid-binding proteins from prokaryotes as vehicles for delivery of materials to eukaryotic cells)

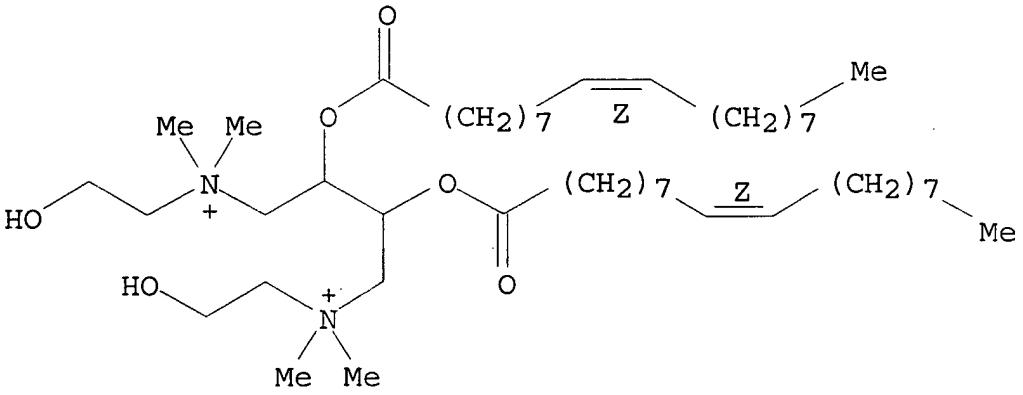
RN 188565-00-6 ZCAPLUS

CN 1,4-Butanediaminium, N,N'-bis(2-hydroxyethyl)-N,N,N',N'-tetramethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, diiodide, mixt. with 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl di-(9Z)-9-octadecenoate (9CI) (CA INDEX NAME)

CM 1

CRN 219304-09-3
CMF C48 H94 N2 O6 . 2 I

Double bond geometry as shown.



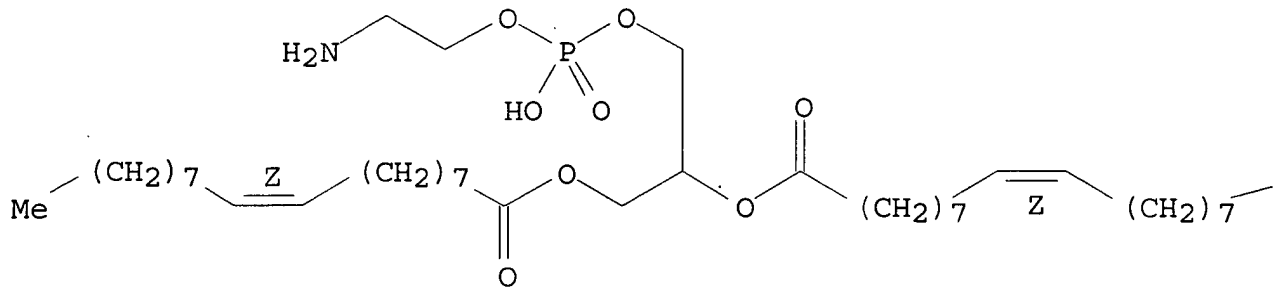
● 2 I^-

CM 2

CRN 2462-63-7
CMF C41 H78 N O8 P

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

IT **188565-00-6**, TFX 50
(liposomes of, contg. protein DNA complexes, for transformation of animal cells; use of nucleic acid-binding proteins from prokaryotes as vehicles for delivery of materials to eukaryotic cells)

L19 ANSWER 8 OF 25 ZCAPLUS COPYRIGHT 2003 ACS
2001:238066 Document No. 134:276493 Cationic virosomes as transfer system for genetic material. Walti, Ernst Rudolf; Gluck, Reinhard; Klein, Peter (Nika Health Products Limited, Liechtenstein). U.S. US 6210708 B1 20010403, 39 pp., Cont.-in-part of U.S. Ser. No. 171,882. (English). CODEN: USXXAM. APPLICATION: US 1999-414872 19991008. PRIORITY: EP 1996-107282 19960508; WO 1997-EP2268 19970504; US 1998-171882 19981230.

AB The present invention relates to a pos. charged virosome for efficient delivery of genetic material to resting or proliferating mammalian cells in vitro and in vivo. The virosome membrane contains cationic and/or polycationic lipids, at least one viral fusion peptide and preferably at least one cell-specific marker, advantageously selected from the group consisting of monoclonal antibodies, antibody fragments F(ab')2 and Fab', cytokines, and growth factors, for a selective detection and binding of target cells. The invention further relates to a method for the manuf. of the novel virosomes and to applications thereof, particularly for the manuf. of pharmaceutical compns. to treat cancer or leukemia.

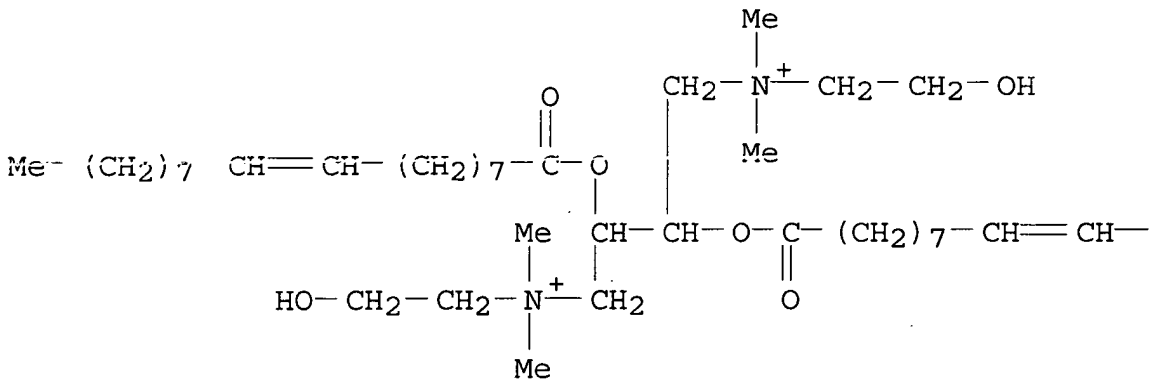
IT **178532-93-9**, THDOB
(lipid bilayer vesicles for cationic virosomes as transfer system

for genetic material)

RN 178532-93-9 ZCAPLUS

CN 1,4-Butanediaminium, N,N'-bis(2-hydroxyethyl)-N,N,N',N'-tetramethyl-2,3-bis[(1-oxo-9-octadecenyl)oxy]-, diiodide (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

— $(CH_2)_7$ — Me

IT **178532-93-9**, THDOB

(lipid bilayer vesicles for cationic virosomes as transfer system for genetic material)

L19 ANSWER 9 OF 25 ZCAPLUS COPYRIGHT 2003 ACS

2000:800664 Document No. 135:961 A hyperthermostable bacterial histone-like protein as an efficient mediator for transfection of eukaryotic cells. Esser, Dirk; Amanuma, Hiroshi; Yoshiki, Atsushi; Kusakabe, Moriaki; Rudolph, Rainer; Bohm, Gerald (Institut fur Biotechnologie, Martin-Luther-Universitat, Halle- Wittenberg, Germany). Nature Biotechnology, 18(11), 1211-1213 (English) 2000. CODEN: NABIF9. ISSN: 1087-0156. Publisher: Nature America Inc..

AB Gene delivery has shown potential in a variety of applications, including basic research, therapies for inborn genetic defects,

cancer, AIDS, tissue engineering, and vaccinations. Most available systems have serious drawbacks, such as safety hazards, inefficiency under in vivo-like conditions, and expensive prodn. When using naked DNA, for instance, a large amt. of ultrapure DNA has to be applied as a result of degrdn. by nucleases. Similarly, the use of eukaryotic histones, synthetic peptides, or peptide nucleic acids may be limited by high prodn. costs. The authors have demonstrated a biotechnol. feasible and economical approach for gene delivery using the histone-like protein from the hyperthermostable eubacterium Thermotoga maritima, TmHU as an efficient gene transfer reagent. HU can be easily isolated from recombinant Escherichia coli, is extraordinarily stable, and protects dsDNA from thermal denaturation. This study demonstrates its use as an inexpensive tool for gene delivery.

IT **188565-00-6**, Tfx 50
(lipofection with; hyperthermostable bacterial histone-like protein as an efficient mediator for transfection of eukaryotic cells)

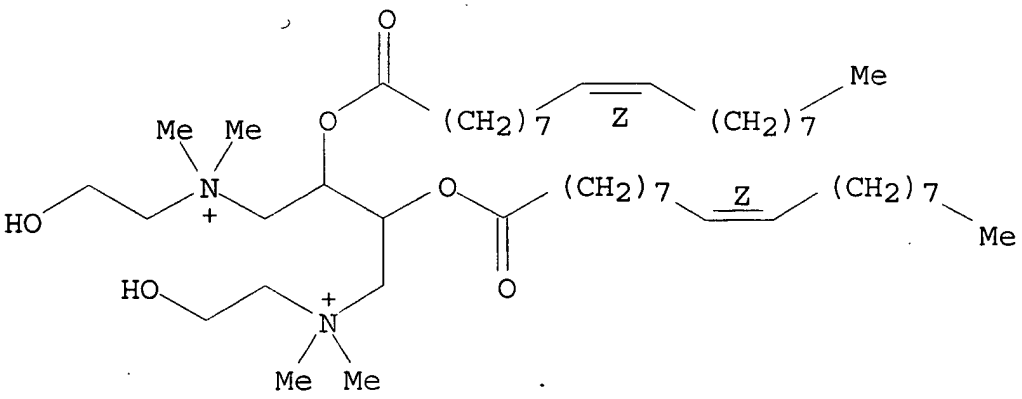
RN 188565-00-6 ZCAPLUS

CN 1,4-Butanediaminium, N,N'-bis(2-hydroxyethyl)-N,N,N',N'-tetramethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, diiodide, mixt. with 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl di-(9Z)-9-octadecenoate (9CI) (CA INDEX NAME)

CM 1

CRN 219304-09-3
CMF C48 H94 N2 O6 . 2 I

Double bond geometry as shown.



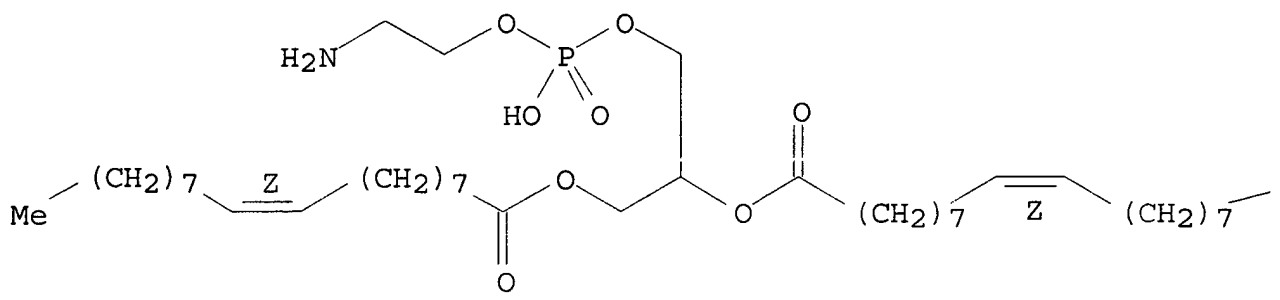
2 I-

CM 2

CRN 2462-63-7
CMF C41 H78 N O8 P

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

IT **188565-00-6**, Tfx 50
(lipofection with; hyperthermostable bacterial histone-like protein as an efficient mediator for transfection of eukaryotic cells)

L19 ANSWER 10 OF 25 ZCAPLUS COPYRIGHT 2003 ACS
2000:678585 Document No. 134:21368 Stable integration of large (> 100 kb) PAC constructs in HaCaT keratinocytes using an integrin-targeting peptide delivery system. Compton, S. H.; Mecklenbeck, S.; Mejia, J. E.; Hart, S. L.; Rice, M.; Cervini, R.; Barrandon, Y.; Larin, Z.; Levy, E. R.; Bruckner-Tuderman, L.; Hovnanian, A. (The Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford, UK). Gene Therapy, 7(18), 1600-1605 (English) 2000. CODEN: GETHEC. ISSN: 0969-7128. Publisher: Nature Publishing Group.

AB Transfer of large DNA constructs in gene therapy studies is being recognized for its importance in maintaining the natural genomic environment of the gene of interest and providing tissue-specific regulation and control. However, methods used to deliver such constructs have been poorly studied. We used a receptor-mediated, integrin-targeting transfection system enhanced by liposomes, to deliver a 110 kb PAC (P1-based artificial chromosome) to HaCaT

keratinocytes. The PAC contained the collagen VII locus, an EGFP (enhanced green fluorescent protein) reporter gene and the puromycin resistance gene (pac) to allow selection of stably transfected cells. Anal. of puromycin resistant and EGFP-expressing colonies by Western blot showed that collagen VII prodn. increased dramatically after transfection, indicating successful transfer of a large fully functional genomic locus. Fluorescent in situ hybridization (FISH) and Southern blot anal. revealed that the PAC had integrated as at least one copy per cell. EGFP expression has persisted for 35 wk, suggesting stable transgene expression. We conclude that the integrin-targeting peptide method of gene delivery is an effective means of stably delivering large DNA constructs to human keratinocytes and could be of benefit for genomic gene therapy approaches.

IT **188565-00-6**, Tfx 10
(stable integration of large PAC constructs in HaCaT keratinocytes using integrin-targeting peptide delivery system)

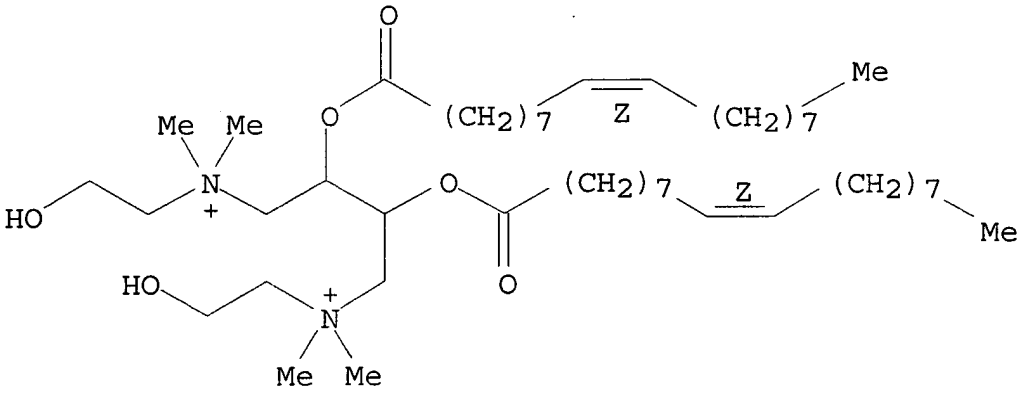
RN 188565-00-6 ZCAPLUS

CN 1,4-Butanediaminium, N,N'-bis(2-hydroxyethyl)-N,N,N',N'-tetramethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, diiodide, mixt. with 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl di-(9Z)-9-octadecenoate (9CI) (CA INDEX NAME)

CM 1

CRN 219304-09-3
CMF C48 H94 N2 O6 . 2 I

Double bond geometry as shown.



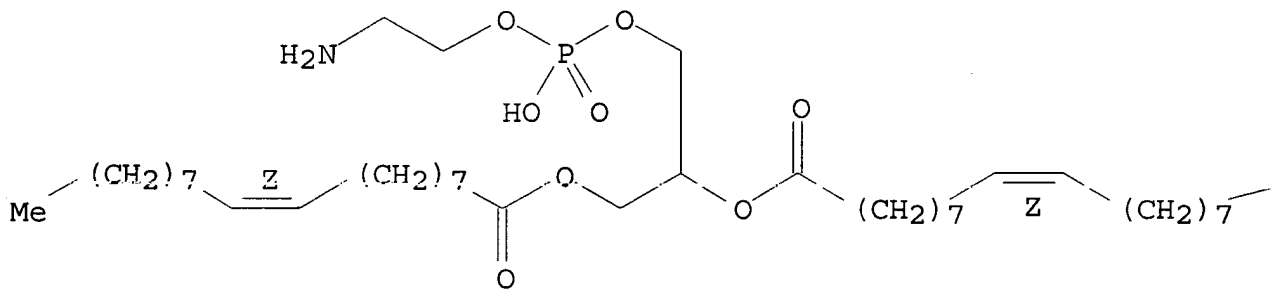
● 2 I⁻

CM 2

CRN 2462-63-7
CMF C41 H78 N O8 P

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

IT **188565-00-6**, Tfx 10
(stable integration of large PAC constructs in HaCaT keratinocytes using integrin-targeting peptide delivery system)

L19 ANSWER 11 OF 25 ZCAPLUS COPYRIGHT 2003 ACS
2000:469092 Document No. 133:202958 Antisense inhibition of IGF receptor expression in HaCaT keratinocytes: a model for antisense strategies in keratinocytes. White, P. J.; Fogarty, R. D.; Werther, G. A.; Wraight, C. J. (Department of Pharmaceutical Biology & Pharmacology, Victorian College of Pharmacy, Monash University, Parkville, 3052, Australia). Antisense & Nucleic Acid Drug Development, 10(3), 195-203 (English) 2000. CODEN: ANADF5. ISSN: 1087-2906. Publisher: Mary Ann Liebert, Inc..

AB Antisense strategies targeting skin conditions are attractive in concept, with a no. of possible pathol. conditions, such a psoriasis, apparently suitable for such an approach. Because in vitro screening of candidate sequences is usually desirable, we have attempted to use a range of new generation cationic lipids to produce significant antisense oligodeoxynucleotide (ODN) uptake in an immortalized keratinocyte cell line (HaCaT). A large no. of com. available lipids were screened for the ability to induce nuclear ODN localization: Tfx-50, Tfx-20, Tfx-10, Superfect, Cytofectin GSV, Perfect lipids 1-8, Lipofectin, and Lipofectamine. All lipids were

used at a range of concns. (1-20 .mu.g/mL) and with a range of ODN concns. (1-1000) nM. Of all lipids used, only Cytofectin GSV and Superfect produced significant (>30% of cells) levels of nuclear pos. cells, with Superfect also producing significant toxicity at the effective concn. used. Only two treatments produced a significant redn. in target mRNA: insulin-like growth factor-1 receptor (IGF-1R)-ODN 64 complexed with Cytofectin GSV (27.1% .+-. 3.5% of IGF-1R mRNA in untreated cells, $p < 0.01$) and ODN 64 complexed with 10 .mu.g/mL Lipofectin (62.2% .+-. 3.4% of IGF-1R mRNA in untreated cells, $p < 0.05$). Only one treatment, ODN 64 complexed with Cytofectin GSV, produced a redn. in cell growth and survival as assessed by amido black assay. These results demonstrate that in HaCaT keratinocytes, Cytofectin GSV alone of all com. available cationic lipids was effective in delivering antisense ODN into cell nuclei such that a profound antisense effect could be demonstrated.

IT **188565-00-6**, Tfx-50
(Tfx 10, Tfx 20; antisense inhibition of IGF receptor expression in HaCaT keratinocytes)

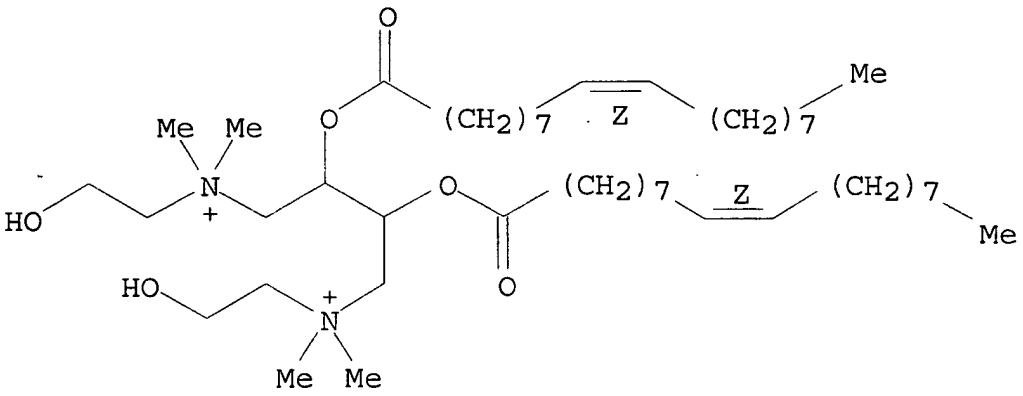
RN 188565-00-6 ZCAPLUS

CN 1,4-Butanediaminium, N,N'-bis(2-hydroxyethyl)-N,N,N',N'-tetramethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, diiodide, mixt. with 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl di-(9Z)-9-octadecenoate (9CI) (CA INDEX NAME)

CM 1

CRN 219304-09-3
CMF C48 H94 N2 O6 . 2 I

Double bond geometry as shown.



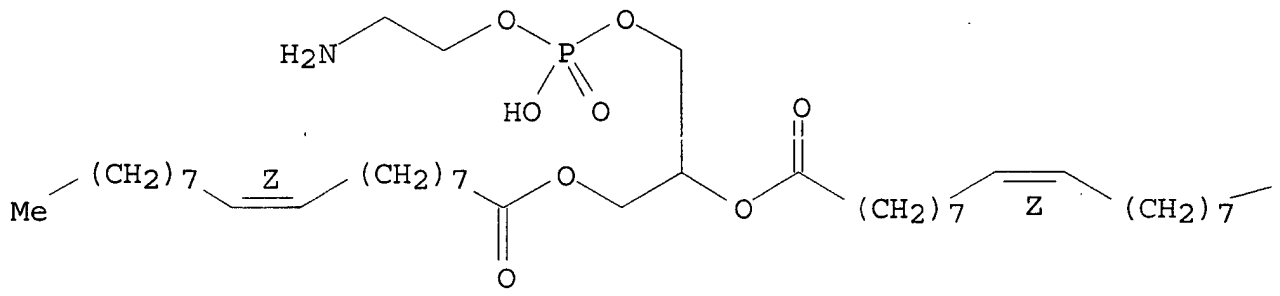
2 I^-

CM 2

CRN 2462-63-7
CMF C41 H78 N O8 P

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

IT **188565-00-6**, Tfx-50
(Tfx 10, Tfx 20; antisense inhibition of IGF receptor expression in HaCaT keratinocytes)

L19 ANSWER 12 OF 25 ZCAPLUS COPYRIGHT 2003 ACS
1999:593365 Document No. 132:88885 Efficient liposome-mediated gene transfer to rabbit carotid arteries in vivo. Keogh, Michael-Christopher; Chen, Daxin (Department of Immunology, Imperial College School of Medicine, London, UK). Methods in Molecular Medicine, 30(Vascular Disease: Molecular Biology and Gene Therapy Protocols), 385-394 (English) 1999. CODEN: MMMEFN. Publisher: Humana Press Inc..

AB Presented is a protocol using the com. available cationic liposome Tfx.RTM.-50 for in vivo gene delivery to rabbit carotid arteries. Procedures are described for the introduction of liposome-plasmid conjugates and immunohistochem. detection of cloned protein. The transfection conditions described here are optimized for gene delivery to rabbit vascular smooth muscle cells.

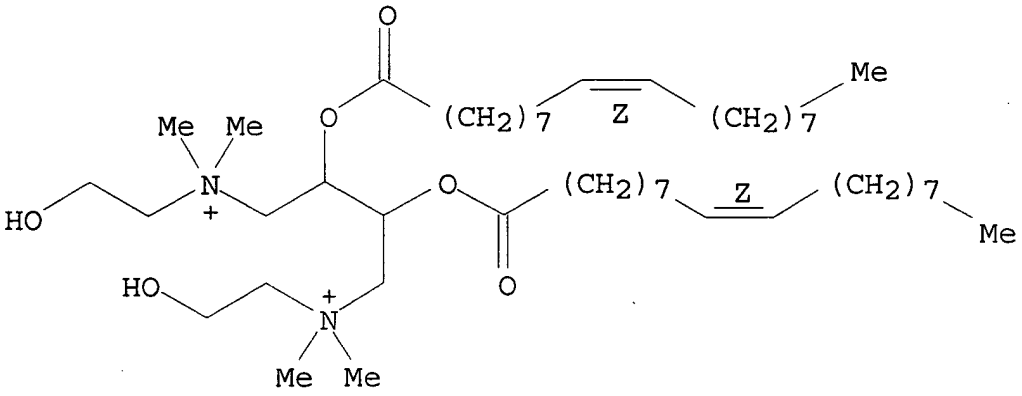
IT **188565-00-6**, Tfx-50
(efficient liposome-mediated gene transfer to rabbit carotid arteries in vivo)

RN 188565-00-6 ZCAPLUS
CN 1,4-Butanediaminium, N,N'-bis(2-hydroxyethyl)-N,N,N',N'-tetramethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, diiodide, mixt. with 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl di-(9Z)-9-octadecenoate (9CI) (CA INDEX NAME)

CM 1

CRN 219304-09-3
CMF C48 H94 N2 O6 . 2 I

Double bond geometry as shown.



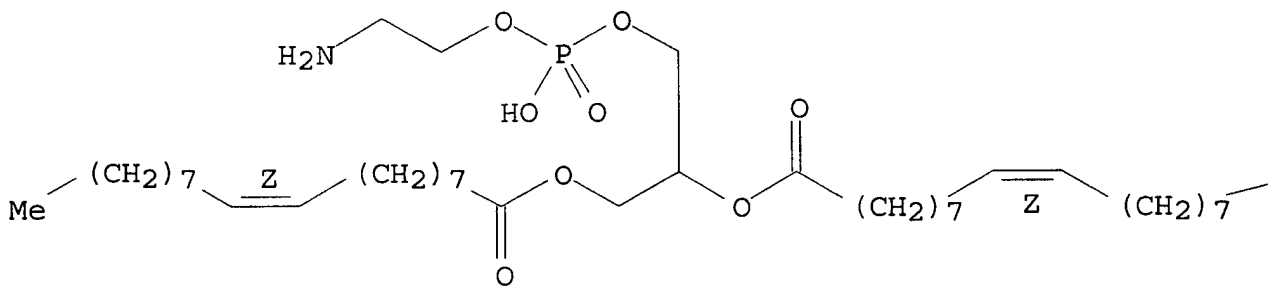
●2 I⁻

CM 2

CRN 2462-63-7
CMF C41 H78 N O8 P

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

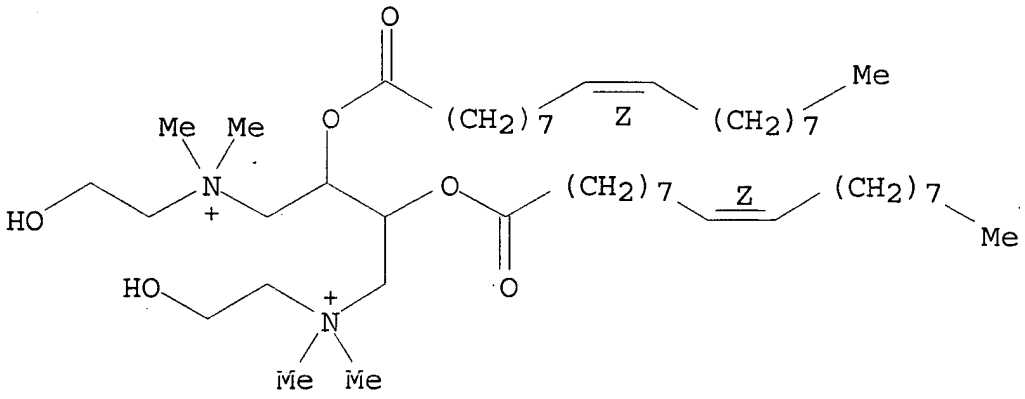
IT **188565-00-6**, Tfx-50
(efficient liposome-mediated gene transfer to rabbit carotid arteries in vivo)

L19 ANSWER 13 OF 25 ZCAPLUS COPYRIGHT 2003 ACS
1999:247078 Document No. 131:83631 Study on transfected ANF gene expression of human leiomyosarcoma cell in vitro. Pan, Shiyang; Ma, Genshan; Huang, Jun; Yang, Chunmei; Huang, Peijun; Tong, Mingqing (Department of Experimental Diagnostic Center, the First Affiliated Hospital, Nanjing Medical University, Nanjing, 210029, Peop. Rep. China). Nanjing Yike Daxue Xuebao, 19(2), 107-110 (Chinese) 1999. CODEN: NYDXFS. ISSN: 1007-4368. Publisher: Nanjing Yike Daxue.
AB Both Tfx-50 liposome coated and uncoated pcDNA3/ANF contg. the human ANF gene were transfected into leiomyosarcoma cells in vitro. The ANF mRNA of the LMS cells was detected by Dot Bloting method using the Dig labeled RNA probe. The ANF peptide levels in the LMS cell culture media were detd. by RIA. The ANF mRNA expression was pos. and the ANF concn. of the cell culture media was up to 58 ng/L when pcDNA3/ANF DNA was coated with Tfx-50 under the charge ratio of 3:1 and the quantity of the DNA was 2.0 .mu.g/105 cell on day 3 after the gene transfection. These indicate that Tfx-50 reagent can be used to enhance pcDNA3/ANF transfection efficiency and gene expression, and it may be used for the study of ANF gene therapy on cardiovascular obstructive disease.
IT **188565-00-6**, Tfx-50
(Tfx-50 liposome coated and uncoated pcDNA3/ANF; transfected atrial natriuretic factor gene expression of human leiomyosarcoma cell in vitro)
RN 188565-00-6 ZCAPLUS
CN 1,4-Butanediaminium, N,N'-bis(2-hydroxyethyl)-N,N,N',N'-tetramethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, diiodide, mixt. with 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl di-(9Z)-9-octadecenoate (9CI) (CA INDEX NAME)

CM 1

CRN 219304-09-3
CMF C48 H94 N2 O6 . 2 I

Double bond geometry as shown.



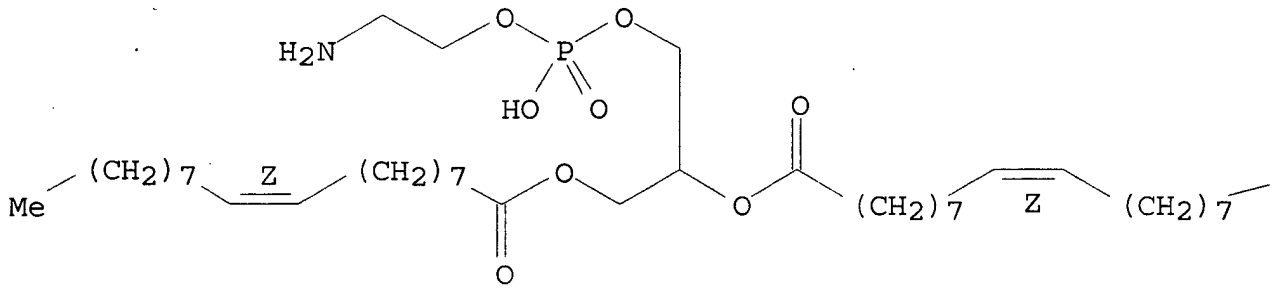
● 2 I^-

CM 2

CRN 2462-63-7
CMF C41 H78 N O8 P

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

IT **188565-00-6**, Tfx-50
(Tfx-50 liposome coated and uncoated pcDNA3/ANF; transfected atrial natriuretic factor gene expression of human leiomyosarcoma cell in vitro)

L19 ANSWER 14 OF 25 ZCAPLUS COPYRIGHT 2003 ACS
1999:231221 Document No. 130:296428 Preparation of bis(acyloxy)alkanediaminium compounds as cationic transport reagents. Nantz, Michael H.; Bennett, Michael J.; Malone, Robert W. (The Reagents of the University of California, USA). U.S. US 5892071 A 19990406, 22 pp., Cont.-in-part of U.S. 5,527,928. (English). CODEN: USXXAM. APPLICATION: US 1995-528733 19950915. PRIORITY: US 1994-316719 19940930.

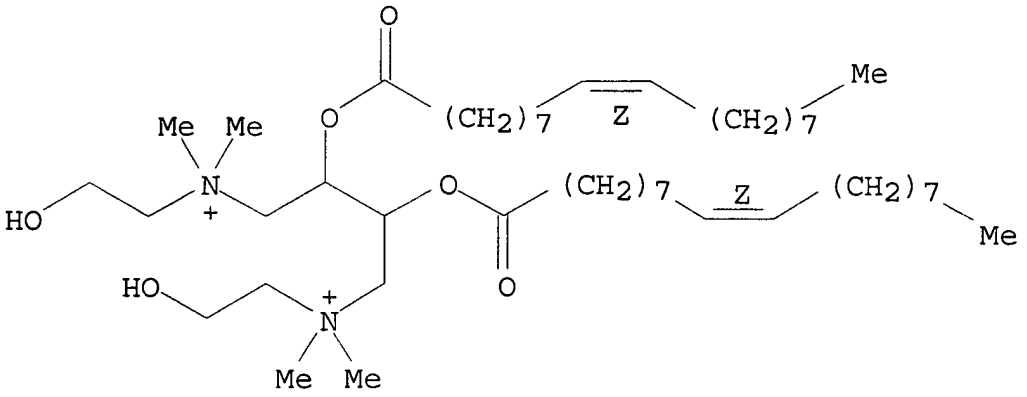
AB The title compds. [R1R3R4N+(CH2)mCH(OR2)]2 2X- (I, m = 1-10; R1 = H, alkyl, alkenyl, hydroxylated alkyl or alkenyl group, or an ether contg. alkyl or alkenyl group; R2 = alkyl, alkenyl, or an alkyl or alkenyl contg. acyl group; R3 = H, alkyl, alkenyl, a hydroxylated alkyl or alkenyl, or an ether contg. alkyl or alkenyl; R4 = H, alkyl, alkenyl, hydroxylated alkyl or alkenyl, or an ether contg. alkyl or alkenyl; X = anion.) were prepd. for transporting biol. active species into and through membrane barriers. Thus, 1,3-butadiene diepoxide was condensed with Me3CPh2SiOCH2CH2NHMe and the product acylated with oleoyl chloride to give, after deprotection and quaternization, I (R1 = R3 = Me, R2 = oleoyl, R4 = CH2CH2OH, X = iodo). Data for activity of I were given in graphic form.

IT **219304-09-3P**
(prepn. of bis(acyloxy)alkanediaminium compds. as cationic transport reagents)

RN 219304-09-3 ZCAPLUS

CN 1,4-Butanediaminium, N,N'-bis(2-hydroxyethyl)-N,N,N',N'-tetramethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, diiodide (9CI) (CA INDEX NAME)

Double bond geometry as shown.



●2 I^-

IT **219304-09-3P**
(prepn. of bis(acyloxy)alkanediaminium compds. as cationic transport reagents)

L19 ANSWER 15 OF 25 ZCAPLUS COPYRIGHT 2003 ACS
1999:194028 Document No. 130:242303 Method of in vivo transformation of central nervous system cells utilizing lipid vehicles. Federoff, Howard J.; Haak-Frendscho, Mary (Promega Corporation, USA). PCT Int. Appl. WO 9912575 A1 19990318, 38 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US18615 19980908. PRIORITY: US 1997-58135 19970908.

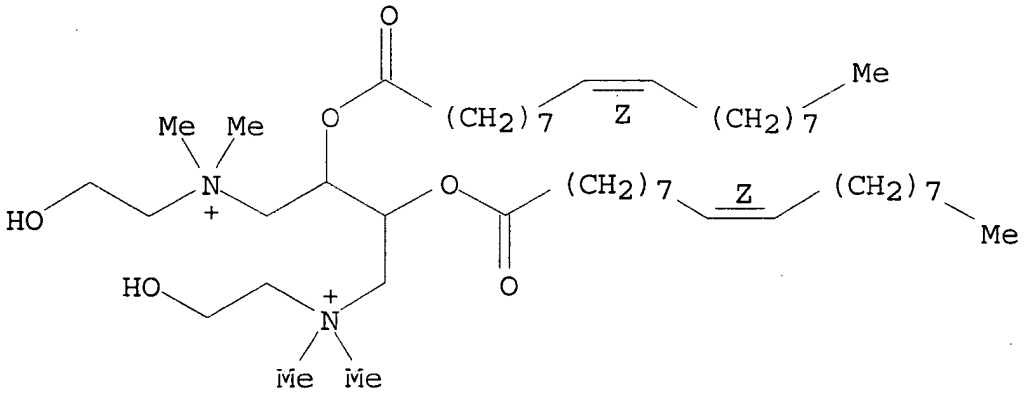
AB An in vivo method for the transformation of central nervous system cells of animals utilizing a transformation reagent contg. an admixt. of a DNA or RNA encoding a gene product of interest and a lipid compn. contg. a fusogenic lipid and a cationic lipid is disclosed.

IT **219304-09-3**
(in vivo transformation of central nervous system cells utilizing lipid vehicles)

RN 219304-09-3 ZCAPLUS

CN 1,4-Butanediaminium, N,N'-bis(2-hydroxyethyl)-N,N,N',N'-tetramethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, diiodide (9CI) (CA INDEX NAME)

Double bond geometry as shown.



2 I^-

IT **219304-09-3**
(in vivo transformation of central nervous system cells utilizing lipid vehicles)

L19 ANSWER 16 OF 25 ZCAPLUS COPYRIGHT 2003 ACS
1998:789045 Document No. 130:24103 An influenza enveloped DNA vaccine. Cusi, Maria Grazia; Gluck, Reinhard; Walti, Ernst (Schweiz. Serum- & Impfinstitut Bern, Switz.). PCT Int. Appl. WO 9852603 A2 19981126, 43 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-EP3050 19980522. PRIORITY: EP 1997-108390 19970523.

AB Described are virosomes comprising cationic lipids, biol. active influenza hemagglutinin protein or biol. active derivs. thereof and nucleic acids encoding antigens from pathogenic sources in their insides, preferably antigens from mumps virus wherein said antigens are derived from conserved external and internal proteins of said virus. Provided are virosomes which may advantageously be formulated as vaccines capable of inducing strong neutralizing antibody and cytotoxic T cell responses as well as protection to pathogenic sources such as a mumps virus. Furthermore, vaccines comprising recombinant DNA derived from DNA encoding conserved external and internal proteins from mumps virus are described. Mol. cloning of hemagglutinin gene, F gene, and nucleocapsid gene of mumps virus, N gene of respiratory syncytial virus, and S or Pre-S1 or Pre-S2 or S ORF gene of hepatitis B virus was described. Also described were prepn. of DOTAP-PC virosomes and DOTAP-PC-PE

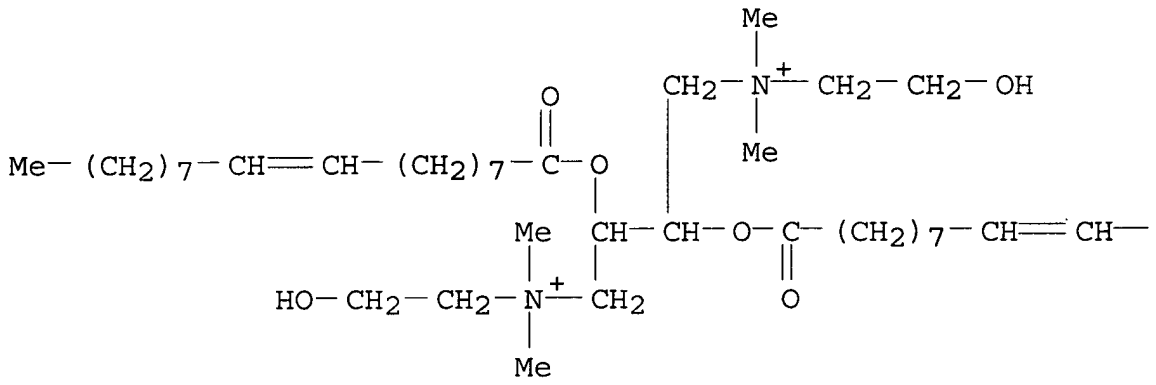
virosomes, incorporation of plasmids expressing mumps genes into DOTAP virosomes, humoral and cellular immune response to viral mumps-antigens induced by genetic immunization.

IT **178532-93-9**, THDOB
(virosomes comprising cationic lipids, influenza hemagglutinin, and antigen gene of pathogen as DNA vaccine for infectious diseases)

RN 178532-93-9 ZCAPLUS

CN 1,4-Butanediaminium, N,N'-bis(2-hydroxyethyl)-N,N,N',N'-tetramethyl-2,3-bis[(1-oxo-9-octadecenyl)oxy]-, diiodide (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

— $(CH_2)_7$ — Me

IT **178532-93-9**, THDOB
(virosomes comprising cationic lipids, influenza hemagglutinin, and antigen gene of pathogen as DNA vaccine for infectious diseases)

L19 ANSWER 17 OF 25 ZCAPLUS COPYRIGHT 2003 ACS

1998:736682 Document No. 130:105808 Optimal lipofection reagent varies with the molecular modifications of the DNA. Conrad, Abigail H.;

Behlke, Mark A.; Jaffredo, Thierry; Conrad, Gary W. (Division of Biology, Kansas State University, Manhattan, KS, 66506-4901, USA). Antisense & Nucleic Acid Drug Development, 8(5), 427-434 (English) 1998. CODEN: ANADF5. ISSN: 1087-2906. Publisher: Mary Ann Liebert, Inc..

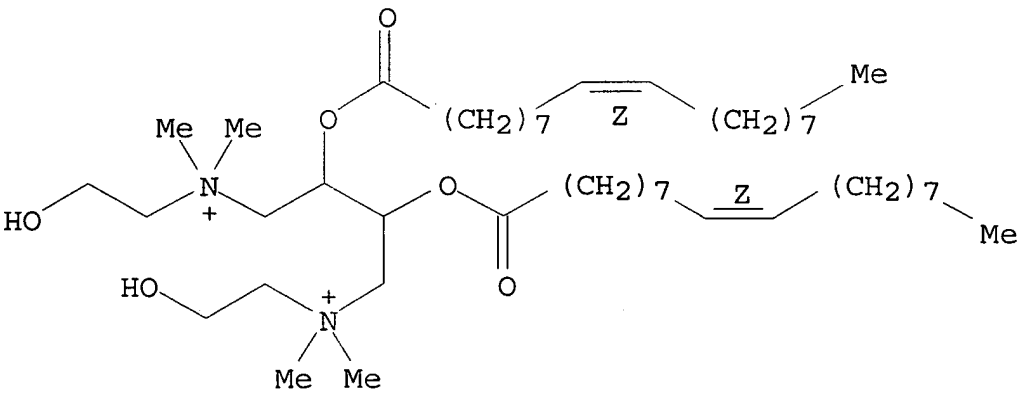
AB Cationic lipid reagents differ in their cytofection efficacy with different cell types. No evidence has addressed whether the same lipid reagent is best for different DNAs in a single cell line. Immortalized avian embryonic cardiomyocytes cultured in vitro were tested with 15 cationic lipid reagents using (A) a .beta.-gal expression plasmid, (B) a fluorescein-tagged, phosphorothioate-modified ODN B, (C) a fluorescein-tagged, ethoxy-modified ODN C with the same nucleotide sequence as ODN B, and (D) a fluorescein-tagged, phosphorothioate-modified ODN D with a different nucleotide sequence from ODNs B and C. Cytofection was scored as percent of cells expressing .beta.-gal activity or showing diffuse cellular fluorescence. The best lipid reagents for the phosphorothioate-modified ODNs were ODN-specific and markedly different from the best lipid reagents for the expression plasmid or for the ethoxy-modified ODN. These results suggest that the best cationic lipid reagent for a particular cell type varies with the phys. and chem. form of the DNA being transfected into the cells.

IT **219304-09-3**
(optimal lipofection reagent varies with mol. modifications of DNA)

RN 219304-09-3 ZCAPLUS

CN 1,4-Butanediaminium, N,N'-bis(2-hydroxyethyl)-N,N,N',N'-tetramethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, diiodide (9CI) (CA INDEX NAME)

Double bond geometry as shown.



2 I^-

IT **219304-09-3**

(optimal lipofection reagent varies with mol. modifications of DNA)

L19 ANSWER 18 OF 25 ZCAPLUS COPYRIGHT 2003 ACS
1998:607505 Document No. 129:341558 Enhanced in vitro and in vivo gene delivery using cationic agent complexed retrovirus vectors. Themis, M.; Forbes, S. J.; Chan, L.; Cooper, R. G.; Etheridge, C. J.; Miller, A. D.; Hodgson, H. J. F.; Coutelle, C. (Division of Biomedical Sciences, Imperial College School of Medicine, London, W2 1PG, UK). Gene Therapy, 5(9), 1180-1186 (English) 1998. CODEN: GETHEC. ISSN: 0969-7128. Publisher: Stockton Press.

AB Retroviruses are, at present, the most efficient integrative vectors available for gene delivery. These viruses are still limited by relatively low titers. Although several protocols exist to improve virus titer most of them are time-consuming and unable to provide sufficient virus for in vivo applications. Virus titer can be enhanced by polybrene and other cationic agents. By investigating a broad range of cationic agents for their ability to enhance virus infectivity the authors found that both ecotropic and amphotropic retrovirus infection could be increased. The lipopolyamine dioctadecylamidoglycylspermine (DOGS) gave .ltoreq. 1 order of magnitude enhancement above polybrene-mediated infection without cytotoxicity. To increase virus infectivity further the authors combined the enhancing effect of DOGS on virus infectivity with concn. of virus particles by ultrafiltration to reach titers of 1 .times. 109 IU/mL. The in vivo transduction of regenerating rat liver, by an amphotropic retrovirus was increased approx. 5-fold by the addn. of DOGS compared with virus alone. There was no animal toxicity obsd. following the administration of DOGS. The improved transduction efficiency seen both in vitro and in vivo following the co-administration of DOGS/virus complexes may be useful for future gene therapy applications.

IT **188565-00-6**, Tfx 50
(enhanced gene delivery using cationic agent complexed retrovirus vectors)

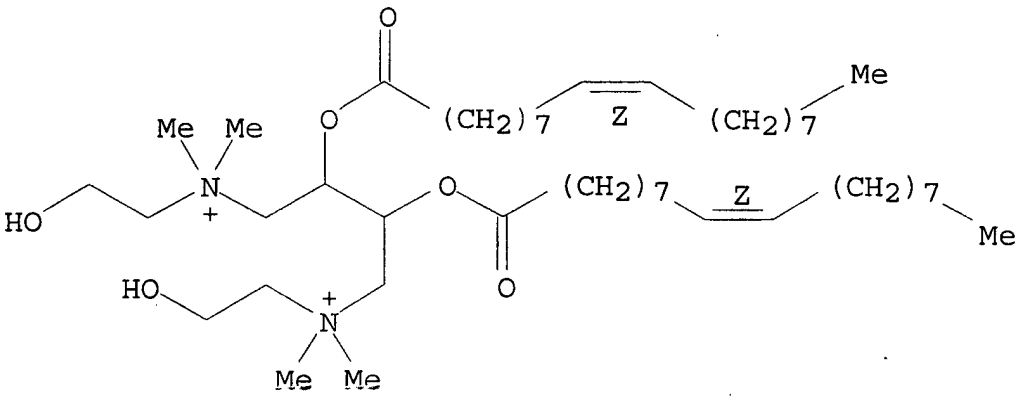
RN 188565-00-6 ZCAPLUS

CN 1,4-Butanediaminium, N,N'-bis(2-hydroxyethyl)-N,N,N',N'-tetramethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, diiodide, mixt. with 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl di-(9Z)-9-octadecenoate (9CI) (CA INDEX NAME)

CM 1

CRN 219304-09-3
CMF C48 H94 N2 O6 . 2 I

Double bond geometry as shown.



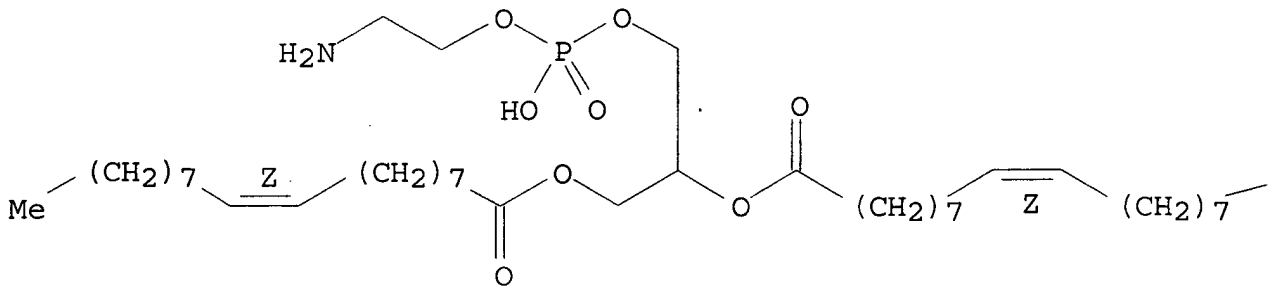
●2 I^-

CM 2

CRN 2462-63-7
CMF C41 H78 N O8 P

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

IT **188565-00-6**, Tfx 50
(enhanced gene delivery using cationic agent complexed retrovirus vectors)

L19 ANSWER 19 OF 25 ZCAPLUS COPYRIGHT 2003 ACS
1998:351793 Document No. 129:36461 Complexes of adenovirus with cationic molecules for gene therapy. Welsh, Michael J.; Fasbender, Allen J. (University of Iowa Research Foundation, USA). PCT Int. Appl. WO 9822144 A2 19980528, 57 pp. DESIGNATED STATES: W: AU, CA, JP; RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US21496 19971120. PRIORITY: US 1996-755035 19961122.

AB Noncovalent complexes of cationic mols. and adenoviral vectors contg. a transgene exhibit increased efficiency of gene transfer to a target cell relative to adenoviral vectors alone. The cationic mol. may be a polymer (e.g. poly-L-lysine, PEI, DEAE-dextran, histone fraction V-S, cationic dendrimer) or a cationic lipid such as N-[(N,N-dimethylamino)ethane]carbamoylcholesterol or N4-spermine cholesterol carbamate. The cystic fibrosis transmembrane conductance regulator (CFTR) may be delivered to a cystic fibrosis patient by applying to the nasal epithelium a complex of poly-L-lysine and an adenoviral vector contg. a transgene encoding a CFTR protein.

IT **188565-00-6**, Tfx-50
(complexes of adenovirus with cationic mols. for gene therapy)

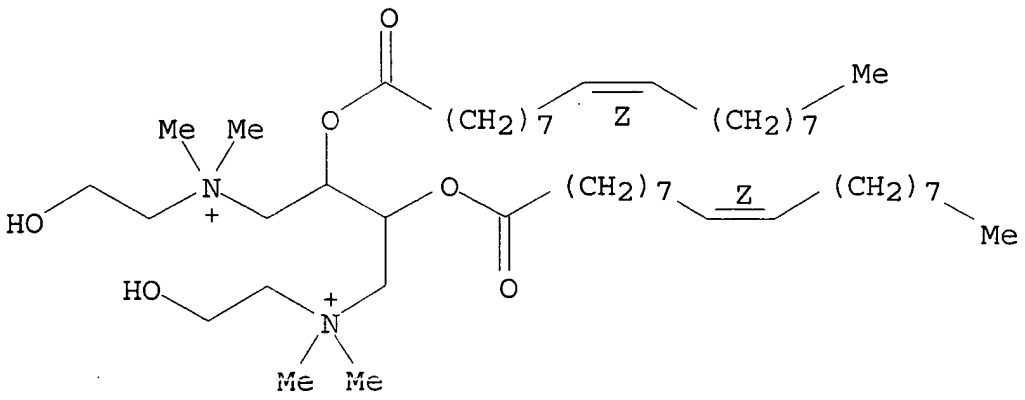
RN 188565-00-6 ZCAPLUS

CN 1,4-Butanediaminium, N,N'-bis(2-hydroxyethyl)-N,N,N',N'-tetramethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, diiodide, mixt. with 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl di-(9Z)-9-octadecenoate (9CI) (CA INDEX NAME)

CM 1

CRN 219304-09-3
CMF C48 H94 N2 O6 . 2 I

Double bond geometry as shown.



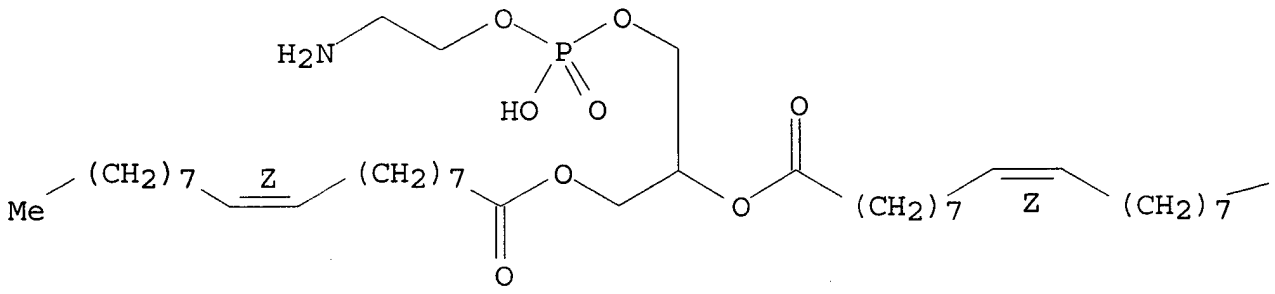
● 2 I^-

CM 2

CRN 2462-63-7
CMF C41 H78 N O8 P

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

IT **188565-00-6**, Tfx-50
(complexes of adenovirus with cationic mols. for gene therapy)

L19 ANSWER 20 OF 25 ZCAPLUS COPYRIGHT 2003 ACS
1997:740426 Document No. 128:53199 Cationic virosomes as transfer system for genetic material. Walti, Ernst Rudolf; Gluck, Reinhard; Klein, Peter (Nika Health Products Limited, Liechtenstein; Walti, Ernst Rudolf; Gluck, Reinhard; Klein, Peter). PCT Int. Appl. WO 9741834 A1 19971113, 52 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-EP2268 19970504. PRIORITY: EP 1996-107282 19960508.

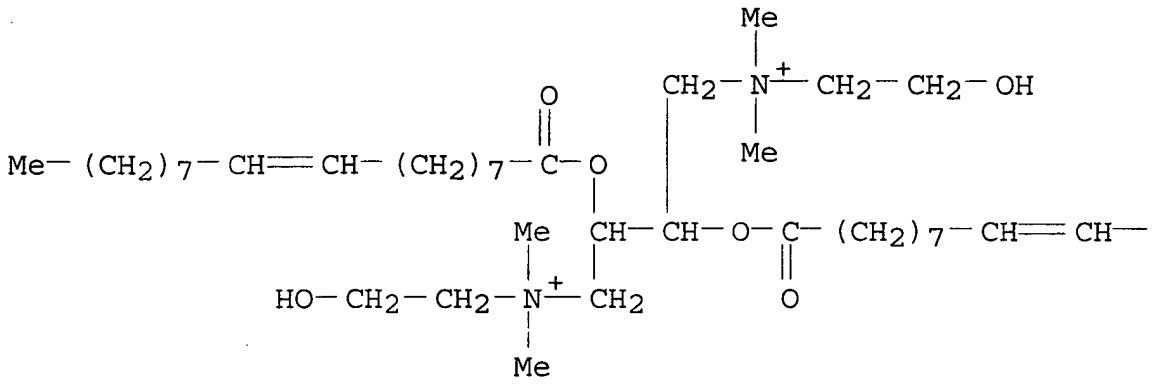
AB The present invention relates to a pos. charged virosome for efficient delivery of genetic material to resting or proliferating mammalian cells in vitro and in vivo. The virosome membrane contains cationic and/or polycationic lipids, at least one viral fusion peptide and preferably at least one cell-specific marker, advantageously selected from the group consisting of monoclonal antibodies, antibody fragments F(ab')2 and Fab', cytokines, and growth factors, for a selective detection and binding of target cells. The invention further relates to a method for the manuf. of the novel virosomes and to applications thereof, particularly for the manuf. of pharmaceutical compns. to treat cancer or leukemia.

IT **178532-93-9**, THDOB
(cationic virosomes as transfer system for genetic material)

RN 178532-93-9 ZCAPLUS

CN 1,4-Butanediaminium, N,N'-bis(2-hydroxyethyl)-N,N,N',N'-tetramethyl-2,3-bis[(1-oxo-9-octadecenyl)oxy]-, diiodide (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

— $(CH_2)_7$ — Me

IT **178532-93-9**, THDOB
(cationic virosomes as transfer system for genetic material)

L19 ANSWER 21 OF 25 ZCAPLUS COPYRIGHT 2003 ACS
1997:384233 Document No. 127:4086 Hormone immunomodulated induction of mucosal immune responses. Mitchell, William M. (Merlin Technologies, Inc., USA). PCT Int. Appl. WO 9714442 A1 19970424, 100 pp. DESIGNATED STATES: W: AU, CA, JP; RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1996-US16845 19961017. PRIORITY: US 1995-544575 19951018.

AB The invention provides a method of inducing a mucosal immune response in a subject, comprising administering to the subject an amt. of antigen-encoding DNA effective to induce a mucosal immune response complexed to a transfection-facilitating cationic lipid and an amt. of vitamin D3. In the method of inducing a mucosal immune response, the antigen-encoding DNA can encode an antigen that is expressed on the surface of transfected cells and mimic crit. elements of infection. DNA encoding the envelope glycoproteins of

viral linked to cationic grouping in which there is coordination of pos. charged groups with a neg. charged phosphate oxygen of the DNA chain forming an ionic charge complex. Two preferred examples of cationic lipids are DOGS (dioctadecylamidoglycylspermidine) and TEDBI (N,N,N',N'-tetramethyl N,N'-bis(2-hydroxyethyl)-2,3-dioleoyloxy-1,4-butane diammonium iodide). The invention also provides a compn., comprising an amt. of DNA encoding an envelope antigen or envelope-assocd. antigen of a pathogen complexed to a cationic lipid. More specifically, the invention provides a compn., comprising an amt. of DNA encoding an envelope antigen of HIV complexed to a cationic lipid.

IT **188565-00-6**, N,N,N',N'-Tetramethyl N,N'-bis(2-hydroxyethyl)-2,3-dioleoyloxy-1,4-butane diammonium iodide
(DNA vaccine encoding envelope antigen and vitamin D3 and transfection-facilitating cationic lipid for induction of mucosal immune responses)

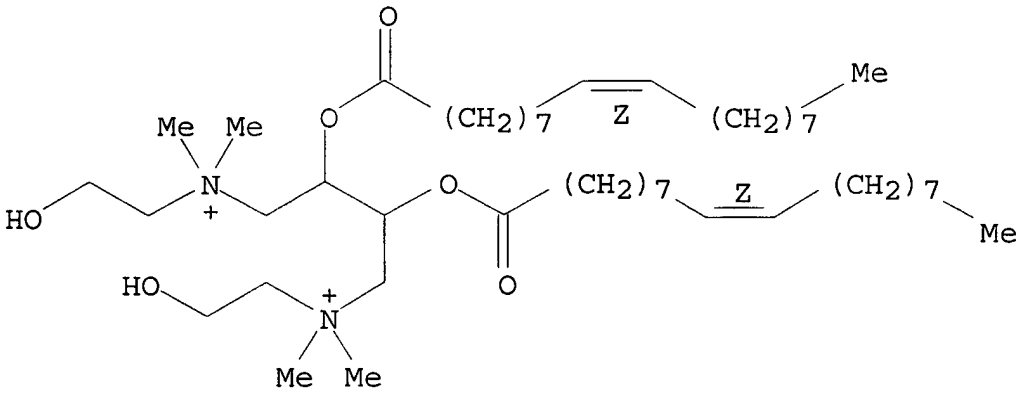
RN 188565-00-6 ZCAPLUS

CN 1,4-Butanediaminium, N,N'-bis(2-hydroxyethyl)-N,N,N',N'-tetramethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, diiodide, mixt. with 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl di-(9Z)-9-octadecenoate (9CI) (CA INDEX NAME)

CM 1

CRN 219304-09-3
CMF C48 H94 N2 O6 . 2 I

Double bond geometry as shown.



●2 I⁻

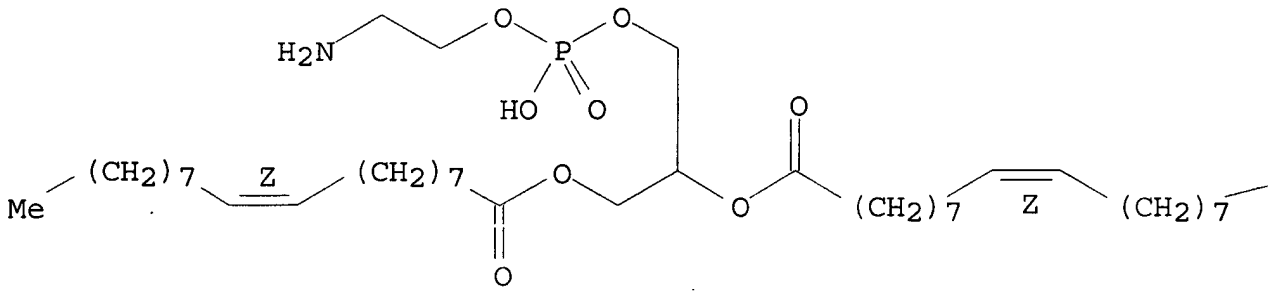
CM 2

CRN 2462-63-7

CMF C41 H78 N O8 P

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

IT **188565-00-6**, N,N,N',N'-Tetramethyl N,N'-bis(2-hydroxyethyl)-2,3-dioleoyloxy-1,4-butane diammonium iodide
(DNA vaccine encoding envelope antigen and vitamin D3 and transfection-facilitating cationic lipid for induction of mucosal immune responses)

L19 ANSWER 22 OF 25 ZCAPLUS COPYRIGHT 2003 ACS
1997:187508 Document No. 126:268364 Complexes of adenovirus with polycationic polymers and cationic lipids increase the efficiency of gene transfer in vitro and in vivo. Fasbender, Al; Zabner, Joseph; Chillon, Miguel; Moninger, Thomas O.; Puga, Aurita P.; Davidson, Beverly L.; Welsh, Michael J. (Dep. Internal Med. and Physiology and Biophysics, Univ. Iowa College Med., Iowa City, IA, 52242, USA). Journal of Biological Chemistry, 272(10), 6479-6489 (English) 1997. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society for Biochemistry and Molecular Biology.

AB Improving the efficiency of gene transfer remains an important goal in developing new treatments for cystic fibrosis and other diseases. Adenovirus vectors and non-viral vectors each have specific advantages, but they also have limitations. Adenovirus vectors efficiently escape from the endosome and enter the nucleus, but the virus shows limited binding to airway epithelia. Nonviral cationic vectors bind efficiently to the neg. charged cell surface, but they do not catalyze subsequent steps in gene transfer. To take

advantage of the unique features of the two different vector systems, we noncovalently complexed cationic mols. with recombinant adenovirus encoding a transgene. Complexes of cationic polymers and cationic lipids with adenovirus increased adenovirus uptake and transgene expression in cells that were inefficiently infected by adenovirus alone. Infection by both complexes was independent of adenovirus fiber and its receptor and occurred via a different cellular pathway than adenovirus alone. Complexes of cationic mols. and adenovirus also enhanced gene transfer to differentiated human airway epithelia in vitro and to the nasal epithelium of cystic fibrosis mice in vivo. These data show that complexes of adenovirus and cationic mols. increase the efficiency of gene transfer, which may enhance the development og gene therapy.

IT **188565-00-6**, Tfx 50
(non-cholesterol-based cationic lipids; adenovirus vector with polycationic polymers and cationic lipids increase efficiency of gene transfer in vitro and in vivo)

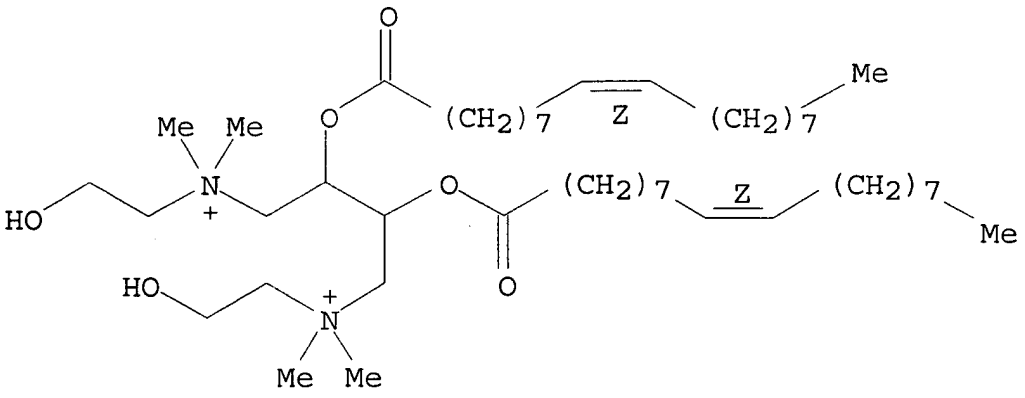
RN 188565-00-6 ZCAPLUS

CN 1,4-Butanediaminium, N,N'-bis(2-hydroxyethyl)-N,N,N',N'-tetramethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, diiodide, mixt. with 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl di-(9Z)-9-octadecenoate (9CI) (CA INDEX NAME)

CM 1

CRN 219304-09-3
CMF C48 H94 N2 O6 . 2 I

Double bond geometry as shown.



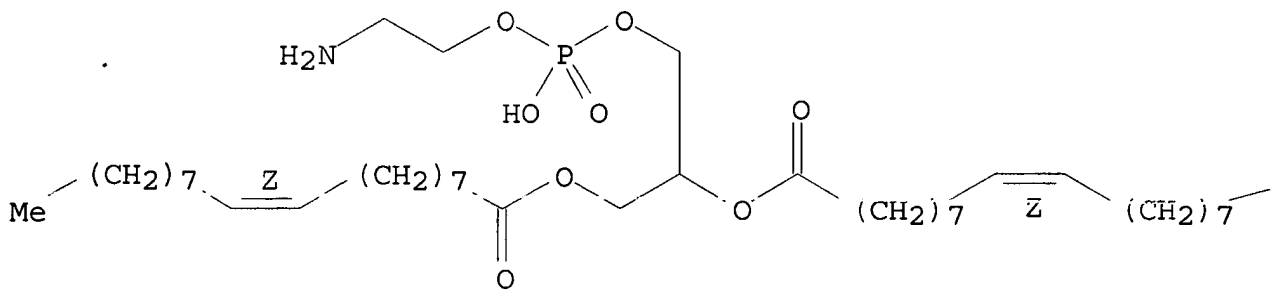
● 2 I⁻

CM 2

CRN 2462-63-7
CMF C41 H78 N O8 P

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

IT **188565-00-6**, Tfx 50
(non-cholesterol-based cationic lipids; adenovirus vector with polycationic polymers and cationic lipids increase efficiency of gene transfer in vitro and in vivo)

L19 ANSWER 23 OF 25 ZCAPLUS COPYRIGHT 2003 ACS
1997:125246 Document No. 126:233046 High efficiency reporter gene transfection of vascular tissue in vitro and in vivo using a cationic lipid-DNA complex. Keogh, M.-C.; Chen, D.; Lupu, F.; Shaper, N.; Schmitt, J. F.; Kakkar, V. V.; Lemoine, N. R. (Thrombosis Res. Inst., London, UK). Gene Therapy, 4(2), 162-171 (English) 1997. CODEN: GETHEC. ISSN: 0969-7128. Publisher: Stockton.

AB Efficient transfection conditions for a no. of human, rat and rabbit primary cells and established lines of vascular origin have been detd. using a complex of a com. available cationic lipid transfection agent (TfxTM-50) and luciferase reporter plasmid constructs. The optimized conditions have also been successfully applied to rabbit carotid arteries in vivo ad a series of human arteries in vitro. The most crit. factors influencing the efficiency of gene transfection with this protocol are: DNA concn.; ratio fo lipid reagent to DNA; transfection time and the presence or absence of serum. Immunohistochem. anal. shows that a high

percentage of cells (approx. 30-80% dependent on lineage) were transfected under optimal conditions with minimal toxicity effects. Similar analyses performed on undamaged rabbit carotid vessels transfected in vivo and human arteries transfected in vitro show high-efficiency transfer and strong expression of the luciferase vector as demonstrated by reporter gene expression. The optimization of gene transfer into vascular cells with this cationic lipid complex will be valuable for mol. studies of genes implicated in cardiovascular diseases and as a possible method of gene delivery with therapeutic intent.

IT **188565-00-6**, Tfx 50
(high efficiency reporter gene transfection of vascular tissue using cationic lipid-DNA complex)

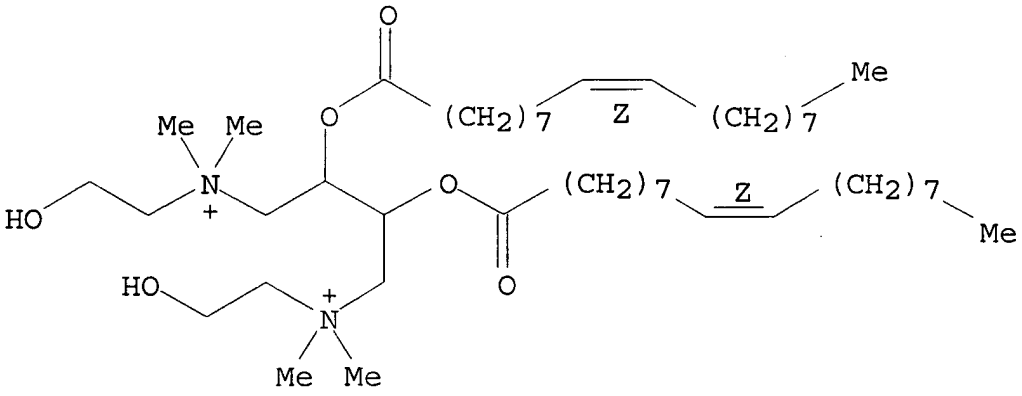
RN 188565-00-6 ZCAPLUS

CN 1,4-Butanediaminium, N,N'-bis(2-hydroxyethyl)-N,N,N',N'-tetramethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, diiodide, mixt. with 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl di-(9Z)-9-octadecenoate (9CI) (CA INDEX NAME)

CM 1

CRN 219304-09-3
CMF C48 H94 N2 O6 . 2 I

Double bond geometry as shown.



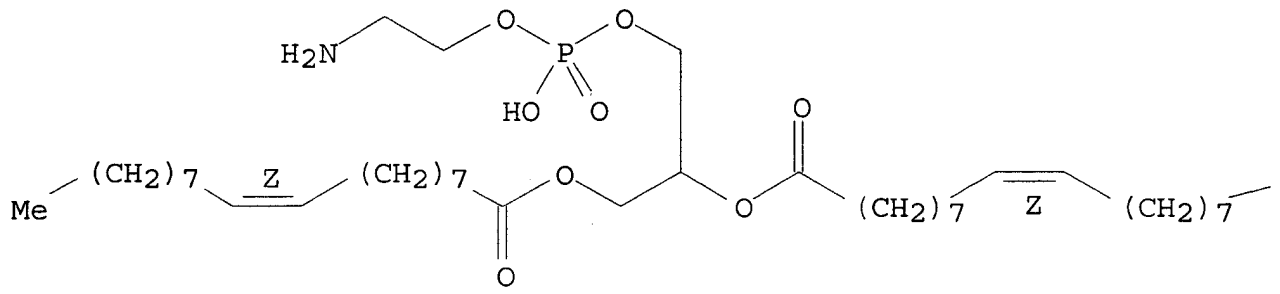
●2 I^-

CM 2

CRN 2462-63-7
CMF C41 H78 N O8 P

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

IT **188565-00-6**, Tfx 50
(high efficiency reporter gene transfection of vascular tissue using cationic lipid-DNA complex)

L19 ANSWER 24 OF 25 ZCAPLUS COPYRIGHT 2003 ACS
1996:446495 Document No. 125:114194 Preparation of bis(acyloxy)alkanediaminium compounds as cationic transport reagents. Nantz, Michael H.; Bennett, Michael J.; Malone, Robert W. (Regents of the University of California, USA). PCT Int. Appl. WO 9610555 A1 19960411, 61 pp. DESIGNATED STATES: W: AU, CA, JP, KR; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1995-US12056 19950921. PRIORITY: US 1994-316719 19940930.

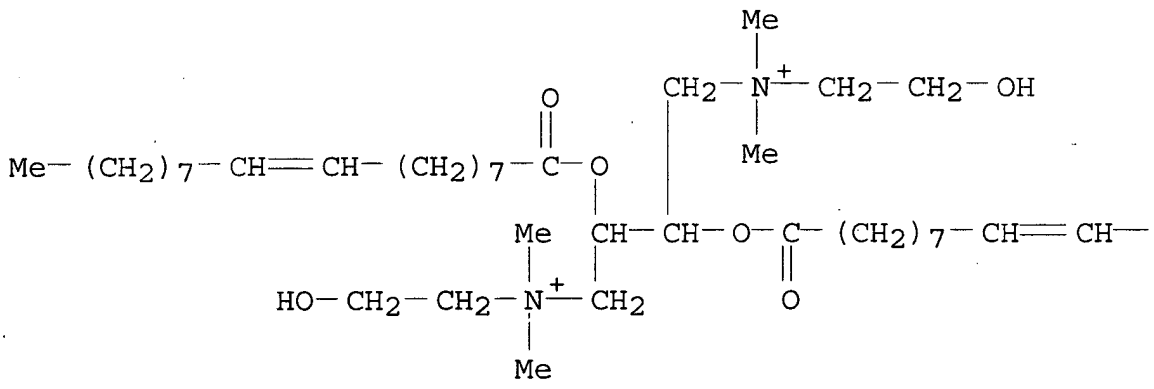
AB Title compds., e.g., [R1R3R4N+(CH2)mCH(OR2)]2 2X- [I; R1, R3, R4 = H, hydroxyalk(en)yl, (O-interrupted) alk(en)yl; R2 = alk(en)yl, acyl, alkenylcarbonyl, etc.; R4 = H, (hydroxylated) alk(en)yl, etc.; X = anion; m = 1-10] were prepd. Thus, 1,3-butadiene diepoxide was condensed with Me3CPh2SiOCH2CH2NHMe and the product acylated with oleoyl chloride to give, after deprotection and quaternization, I (R1 = R3 = Me, R2 = oleoyl, R4 = CH2CH2OH, X = iodo). Data for activity of I were given in graphic form.

IT **178532-93-9P**
(prepn. of bis(acyloxy)alkanediaminium compds. as cationic transport reagents)

RN 178532-93-9 ZCAPLUS

CN 1,4-Butanediaminium, N,N'-bis(2-hydroxyethyl)-N,N,N',N'-tetramethyl-2,3-bis[(1-oxo-9-octadecenyl)oxy]-, diiodide (9CI) (CA INDEX NAME)

PAGE 1-A



2 I^-

PAGE 1-B

— $(CH_2)_7$ — Me

IT **178532-93-9P**
(prepn. of bis(acyloxy)alkanediaminium compds. as cationic transport reagents)

L19 ANSWER 25 OF 25 ZCAPLUS COPYRIGHT 2003 ACS
1996:333351 Document No. 125:67534 DOSPER liposomal transfection reagent: a reagent with unique transfection properties. Buchberger, B.; Fernholz, E.; Bantle, E.; Weigert, M.; Borowski, E.; Eltz, H. v.d.; Hinzpeter, M. (Boehringer Mannheim GmbH, Penzberg, Germany). Biochemica (2), 7-10 (English) 1996. CODEN: BIOCFE. ISSN: 0946-1310. Publisher: Boehringer Mannheim.

AB A novel polycationic lipid, DOSPER [01,3-dioleoyloxy-2-(6-carboxyspermyl)-Pr amide], was synthesized, formulated, and characterized for its applicability as a liposomal transfection reagent. Compared to other com. available liposomal reagents, it showed superior transfection efficiency. Lipofection with DOSPER Liposomal Transfection Reagent was equally effective in the presence or absence of serum. Interestingly, optimal conditions were

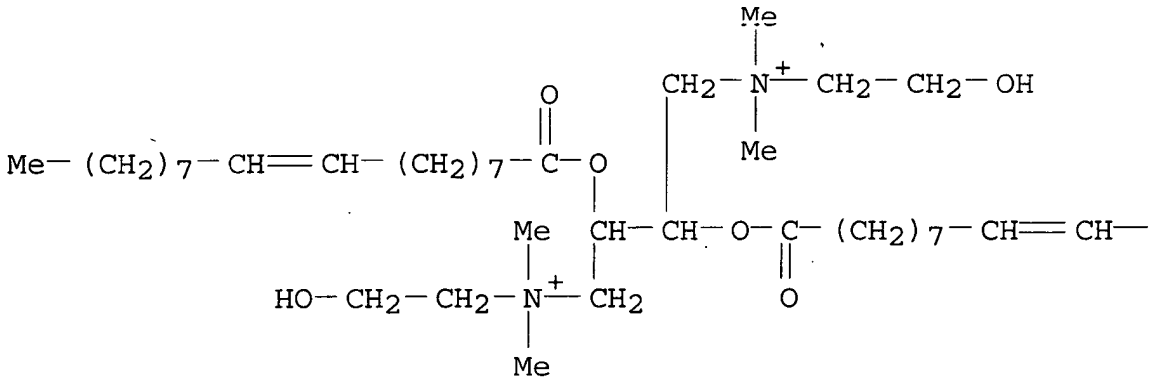
obtained at relatively low concns., which is cost-effective and beneficial with respect to cytotoxic side effects assocd. with most liposomal reagents.

IT **178532-93-9**, THDOB
(transfection system; characterization of DOSPER liposomal transfection reagent)

RN 178532-93-9 ZCAPLUS

CN 1,4-Butanediaminium, N,N'-bis(2-hydroxyethyl)-N,N,N',N'-tetramethyl-2,3-bis[(1-oxo-9-octadecenyl)oxy]-, diiodide (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

— $(CH_2)_7$ — Me

IT **178532-93-9**, THDOB
(transfection system; characterization of DOSPER liposomal transfection reagent)